VOLUME 62 NUMBER 1

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VOLUME 62 JULY 1950 NUMBER 1

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SOLAR DERMATITIS

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SOLAR dermatitis may be defined as an acute or chronic inflammatory reaction of the skin to sunlight. It is characterized by an eruption consisting of pruriginous plaquelike, erythematous, urticarial, papular and vesicular lesions, occurring usually on exposed areas. The lesions undergo exacerbations during the summer, but winter remissions are common. In regions such as Texas, where winters are short, patients may experience no winter remissions. In seasons when snow remains on the ground for some time the reflected light evokes exacerbations.

As would be expected, the patients are for the most part outdoor workers, such as farmers, engineers, surveyors, postmen, oil field workers and stockmen. In many persons who drive a car constantly in their work the eruption is often limited to the left side of the face and neck. In the indoor workers, the use of fluorescent lighting has been thought to provoke the eruption as well as prolong it.

In the Southwest this form of dermatitis is a common diagnostic problem, for here the number of clear and only partly cloudy days is significantly higher than in northern regions in approximately the same longitude. The United States Weather Bureau statistics reveal that in 1947 the number of clear days in Oklahoma City was 161, and in Dallas, Texas, 156, while in Minneapolis it was only 85. The role which heat plays as a cause of solar dermatitis is not clear, but the mean monthly temperature is also significantly higher in the southwestern cities (Oklahoma City, 60.2 F.; Dallas, 65.2 F.; Minneapolis, 45.9 F).

Since 1940, 145 patients with solar dermatitis have been seen in two southwestern centers, Oklahoma City and Dallas. Since 1946, 34 of

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these persons have been studied at the University of Oklahoma School of Medicine with reference to the histopathology of the skin lesions, urinary creatine-creatinine and 17-ketosteroid excretion. On 7 of the men seminal studies have been done. Porphyrin determinations were done on 15 patients. To eliminate the possibility of photosensitization by weeds plus sunlight, patch tests were carried out on 50 patients by the Texas workers, and on 15 patients in Oklahoma City.

There is overlapping of the clinical variants, with transitional stages and combinations of the different types of lesions which have been classified by Rasch [1] and Hausmann and Haxthausen [2] as polymorphic light-sensitive eruptions.

The following working classification has been adopted for the series of patients reported on here:

A. Polymorphic light-sensitive eruptions
   1. Plaquelike type
   2. Contact eczematous type
   3. Papular and prurigo-like type
   4. Erythematous type (erythema solare perstans)

B. Solar urticaria
   1. Reactions to wavelengths of less than 3,700 angstrom units (Beinhauer,[3] Blum, Baer and Sulzberger [4] and Beale [5])
   2. Reactions to wavelengths of 4,000 to 5,000 angstrom units (Ward,[6] Ochs,[7] Blum and West,[8] Arnold [9] and Blum, Barksdale and Green [10])
   3. Nonconfluent urticarial reactions to infra-red radiation of wavelengths between 7,900 and 14,000 angstrom units (Watkins [11])

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1. Rasch, C.: Effect of Light on Skin and Skin Diseases, Proc. Roy. Soc. Med. (Sect. Dermat.) **20**:1, 1926.

2. Hausmann, W. and Haxthausen, H.: Die Lichterkrankungen der Haut: Strahlentherapie, Sonderbände, Berlin, Urban & Schwarzenberg, 1929, vol. 11.

3. Beinhauer, L. G.: Urticaria Solaris, Arch. Dermat. & Syph. **12**:62 (July) 1925.

4. Blum, H. F.; Baer, R. L., and Sulzberger, M. B.: Studies in Hypersensitivity to Light: Urticaria Solare ($\lambda < 3700$), J. Invest. Dermat. **7**:99, 1946.

5. Beale, P.: Studies in Solar Urticaria, J. Invest. Dermat. **11**:415, 1948.

6. Ward, S. B.: Erythema and Urticaria with a Condition Resembling Angioneurotic Oedema Caused Only by Exposure to the Sun's Rays, New York M. J. **81**:742, 1905.

7. Ochs, B. F.: A Case of Urticaria Caused by the Sun's Rays, M. Rec. **78**:193, 1910.

8. Blum, H. F., and West, R. J.: Studies of an Urticarial Response to Blue and Violet Light in Man, J. Clin. Investigation **16**:261, 1937.

9. Arnold, H. L., Jr.: Urticaria Solaris: Review of Literature and Report of Case, Arch. Dermat. & Syph. **43**:607 (April) 1941.

10. Blum, H. F.; Barksdale, E. E., and Green, H. G.: Urticaria Solare (λ 4000-5000 Å), J. Invest. Dermat. **7**:109, 1946.

11. Watkins, A. L.: Infra-red Urticaria, Arch. Phys. Therapy **21**:291, 1943.

C. Rare types
   1. Hydroa vacciniforme with porphyrinuria
   2. Hydroa vacciniforme without porphyrinuria
   3. Epidermolysis bullosa–like lesions with porphyrinuria (Cerutti,[12] Turner and Obermayer [13] and Brunsting and Mason [14])

PLAQUELIKE TYPE OF POLYMORPHIC LIGHT-SENSITIVE ERUPTION

Approximately 75 per cent of the patients with solar dermatitis presented plaquelike lesions. Few references to this variant of polymorphic light-sensitive eruptions are to be found in the literature. Turner [15]

Fig. 1.—Plaquelike types of polymorphic light-sensitive eruptions. Predilection for the posterior aspect of the cheek and the side of the neck may be observed.

reported, in a man 41 years of age, an example of polymorphic light-sensitive eruption of the type to be described.

12. Cerutti, P.: Contributo allo studio dell' epidermolisi bollosa, Gior. ital. di dermat. e. sif. **74**:335, 1933; cited by Blum, H. F.: Photodynamic Action and Diseases Caused by Light, New York, Reinhold Publishing Corporation, 1941, p. 234.

13. Turner, W. J., and Obermayer, M. E.: Studies on Porphyria: II. A Case of Porphyria Accompanied by Epidermolysis Bullosa, Hypertrichosis and Melanosis, Arch. Dermat. & Syph. **37**:549 (April) 1938.

14. Brunsting, L. A., and Mason, H. L.: Porphyria with Epidermolysis Bullosa: Report of Case of Tardive Congenital Type with Demonstration of Latent Porphyria in Sister of Patient, J. A. M. A. **132**:509 (Nov. 2) 1946.

15. Turner, W. J.: Chronic Polymorphous Light Dermatitis with Report of a Case, M. Bull. Vet. Admin. **15**:270, 1939.

Of the 19 patients in this group of the series of 34, all were men, ranging in age from 30 to 59. The average age at onset was 41 years.

The commonest sites of this eruption are the areas normally exposed to sunlight: the cheeks, sides of the neck below the mastoid regions and the V of the neck. All exposed areas may be involved, or the eruption may be limited to certain sites.

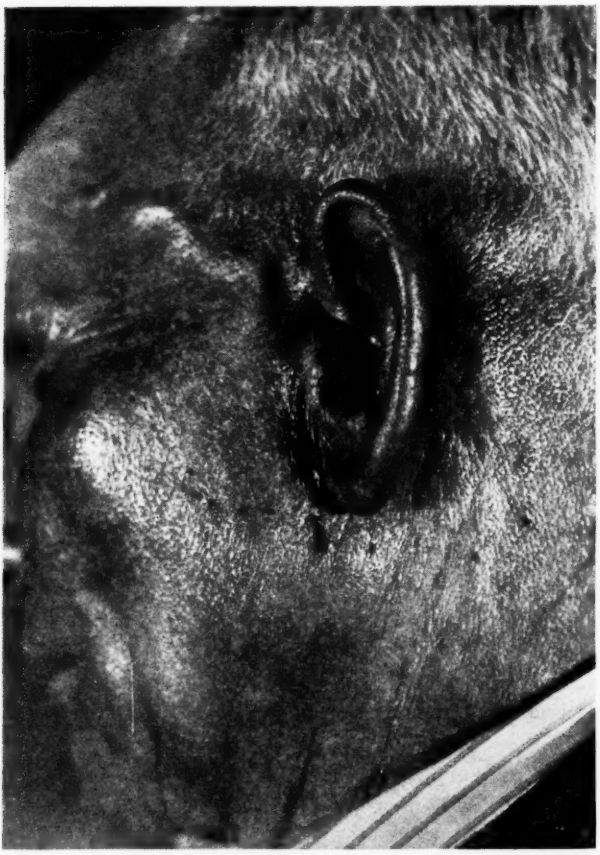

Fig. 2.—Plaquelike type of solar dermatitis behind and below ear, showing hyperpigmentation at the edges of the plaques with depigmentation in the plaques.

The lesions range from 2 cm. in diameter to large plaques (fig. 1) 4 to 5 cm. in diameter. They present a pinkish color in contrast to the tanned hyperpigmented surrounding skin and are in many instances excoriated, lichenified and scaly. Telangiectases are evident over the surface, and induration which extends to a depth of 2 to 3 mm. is

apparent. Initially, some patients may have a papular eruption, the involved skin later becoming thickened and leathery. Pruritus which lasts for variable periods may occasionally be the first symptom, and scratching may cause the induration. Many of the patients show prurigo-like and vesicular lesions concurrently and, in some instances, follicular dilatation. In the winter remission, there is complete disap-

Fig. 3.—Prurigo aestivalis in mother and son. The onset in each case was at 5 years of age.

pearance of the induration and, frequently, subsequent depigmentation of the involved area with surrounding hyperpigmentation of the uninvolved skin (fig. 2). A reticulated pigmentary disturbance resembling poikiloderma of Civatte is frequently observed on the sides of the neck. No atrophy is apparent.

CONTACT ECZEMATOUS TYPE OF POLYMORPHIC LIGHT-SENSITIVE ERUPTION

Two types of contact eczematous solar dermatitis are encountered: diffuse and localized. In both types, the skin is erythematous, pruritic, thickened and excoriated. After a prolonged exposure to the sun, the affected sites become edematous and covered with fine vesicles followed by oozing and crusting (fig. 3).

In the diffuse type, all exposed areas are involved: the face, neck, backs of the hands, even the dorsal surfaces of the forearms if the sleeves are worn rolled to the elbows and the legs if this site is not protected from sunlight. The submental triangle is spared. On the sides and posterior surface of the neck the eruption is sharply delimited by the collar line. Patients are usually well aware of their sensitivity and protect their skin with wearing apparel.

In the localized type of eczematous solar dermatitis only certain exposed areas are involved, usually the cheeks or the cheeks and the chin. The sides and posterior surface of the neck may or may not be affected. Even when not protected by gloves, the backs of the hands may be free of the eruption. In the localized type the skin in different regions does not seem to be equally sensitive. Local variations in photosensitivity were described by Blum,[16] who found that the photosensitivity of different parts of the body varies widely. The abdomen and lumbar regions are more than twenty times as sensitive as the face and hands.

PAPULAR AND PRURIGO-LIKE TYPE OF POLYMORPHIC LIGHT-SENSITIVE ERUPTION

Only 1 patient in whom papular prurigo-like lesions predominated was encountered in the series of 34 cases. Most of the other types of polymorphic light-sensitive eruptions present pruriginous lesions.

Prurigo aestivalis, or Hutchinson's summer prurigo, is characterized by recurrent eruptions of prurigo-like papules and nodules on the areas exposed to the light: the face, neck, hands and arms, the V of the neck and sometimes the lower parts of the legs (fig. 4). The dermatologic picture is varied and may change in the same patient. The first symptom is usually burning and itching of the skin followed by erythema and some degree of urticaria-like swelling. There is considerable confusion in the differential diagnosis of prurigo aestivalis and hydroa vacciniforme.

In prurigo aestivalis the areas of involvement are diffuse and if on the face the lesions usually involve the entire cheek and sides of the neck. In counterdistinction, the lesions of hydroa vacciniforme follow a certain distinct discrete line on points of the most intense solar exposure: the top of the ears, the malar region and the area over the bridge of the nose.

16. Blum, H. F.: Photodynamic Action and Diseases Caused by Light, American Chemical Society Monograph Series, no. 85, New York, Reinhold Publishing Corporation, 1941, p. 201.

The lesions of prurigo aestivalis on the arms are lichenified and diffusely pruriginous as opposed to the more or less discrete lesions of a typical case of hydroa vacciniforme, with or without excoriation and lichenification. In some cases the lesions seem to be more vesicular than papular, and these cases grade into the contact eczematous group. Epstein [17] referred to a confluence of several lesions as "prurigo à grosses papules."

Pick [18] was the first to call attention to the fact that hydroa vacciniforme has its onset in early childhood, while prurigo aestivalis begins at a later age. Epstein [18a] pointed out that this is not a valid criterion since about one third of the cases of hydroa vacciniforme begin before the third year of life and about four fifths before the fourteenth year and many cases of prurigo aestivalis start in childhood (fig. 2).

Pick [18] emphasized the predominant occurrence of hydroa vacciniforme in the male, and prurigo aestivalis in the female. However, Senear and Fink,[19] in their extensive review of 80 cases of hydroa vacciniforme, found the ratio to be 2 to 1 in favor of the female sex. In our series of 3 published cases [20] and 2 subsequently studied, 3 patients were male and 2 were female.

Pick [18] pointed out the fact that hydroa vacciniforme produces scarring and that in prurigo aestivalis the skin heals without scarring. However, others have observed that mild eruptions of hydroa vacciniforme may frequently heal without scars and that cases of prurigo aestivalis tend to leave scars.

A further differentiation which Goeckerman and associates [21] suggested is that most cases of hydroa vacciniforme tend to disappear at puberty and that prurigo aestivalis persists throughout life. We have observed, for two years, 2 boys with hydroa vacciniforme in whom the lesions failed to clear at puberty.

As Epstein [18a] concluded, typical cases of either condition may present easily recognizable clinical entities. However, there is no single criterion which will serve as a cardinal sign in differentiation.

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17. Epstein, S.: Studies of Abnormal Human Sensitivity to Sight: II. Light Sensitivity in Prurigo Aestivalis, Eczema Solare and Urticaria Photogenica, J. Invest. Dermat. **5**:225, 1942.

18. Pick, E.: Zur Kenntnis der Sommerprurigo (Hutchinson), Arch. f. Dermat. u. Syph. **146**:466, 1923-1924.

18a. Epstein, S.: Studies in Abnormal Human Sensitivity to Light: I. Prurigo Aestivalis, Eczema Solare and Urticaria Photogenica, J. Invest. Dermat. **5**:187, 1942.

19. Senear, F. E., and Fink, H. W.: Hydroa Vacciniforme Seu Aestivale, Arch. Dermat. & Syph. **7**:145 (Feb.) 1923.

20. Lain, E. S.; Lamb, J. H.; Keaty, C., and Hellbaum, A. A.: The Use of Steroid and Gonadotropic Hormones in Hydroa Vacciniforme, South, M. J. **41**:1041, 1948.

21. Goeckerman, W. H.; Osterberg, A. E., and Sheard, C.: Eczema Solare in a Case of Hematoporphyrinuria, Arch. Dermat. & Syph. **20**:501 (Oct.) 1929.

ERYTHEMATOUS TYPE OF POLYMORPHIC LIGHT-SENSITIVE ERUPTION (ERYTHEMA SOLARE PERSTANS)

A rare group of light-sensitive persons, who complained of erythema without urticaria after the mildest exposure to sunlight, was observed by one of us (B.S.). The eruption appeared ten to fifteen minutes after exposure and frequently disappeared within one hour. Its appearance resembled the flushing of the face and neck after excitement.

In addition to this group of patients showing transient eruptions, 10 patients of the 34 in the series reported showed erythema multiforme–like lesions or erythema solare perstans. In 1 instance confluence of erythema solare perstans involved the entire surface of both cheeks, large areas on the sides of the neck and the skin of the entire forehead.

The early lesions are discrete and are confined to the cheeks, sides of the neck and forehead. They are papular, multiform and urticarial.

TABLE 1.—*Incidence and Distribution of Lesions*

Type of Lesion	No. of Patients	Average Age	Anatomic Distribution		
			Face	Neck	Hand and Forearm
Plaquelike	19	49	15	12	6
Contact eczematous	4	42	4	2	4
Prurigo-like	1	49	0	1	1
Erythema multiforme–like	10	43	6	7	4

They are persistent and not transient, as is true urticaria solare. The lesions range from 1.5 cm. to 3 to 4 cm. in diameter. Differentiation from the evanescent, multiform type of lupus erythematosus is difficult, but there is a definite seasonal remission which is not observed in the multiform type of lupus erythematosus. The lesions are dark pink and not as violaceous as those of lupus erythematosus. The white and red blood cell counts, the albumin-globulin ratio and the sedimentation rate are in normal range in the multiform type of solar dermatitis, whereas many of the evanescent types of lupus erythematosus usually show leukopenia, secondary anemia and reversal of the albumin-globulin ratio.

The incidence and distribution of the four types of lesions are presented in table 1.

HISTOPATHOLOGY

Biopsy specimens were obtained before any treatment was instituted in 28 of the 34 cases included in this study. All were from exposed areas of the body: fourteen from the face, twelve from the neck, one from the chest and one from the hand. In order not to prejudice the pathologist by clinical impressions, the specimens were sent to the laboratory without

any indication of the clinical diagnosis, and only when they had all been assembled and described was any comparison with the clinical differentiations made.

Fifteen of the specimens were from lesions of the plaquelike type. In twelve of these the epidermis as a whole was atrophic, but in all but one there was relative hyperkeratosis. However, small areas of parakeratosis were also present in four. Hair follicles were plugged and distended with keratin. There was some degree of either intercellular or intracellular edema, or both, in the epidermis of ten of the specimens. Small

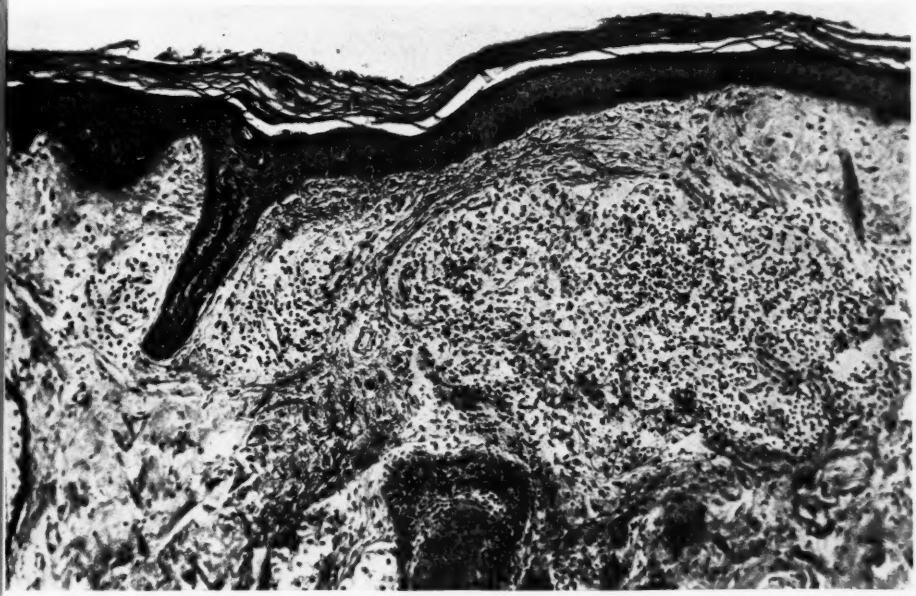

Fig. 4.—Polymorphic light-sensitive eruption, plaquelike type, skin of the neck. The epidermis is atrophic, but there is relatively pronounced hyperkeratosis. The dermis is edematous, and a perivascular cellular infiltrate is present.

areas of liquefaction degeneration of the basal layer, such as are found in biopsy specimens from cases of lupus erythematosus, were present in only five of these. There was no conspicuous increase in pigment in the basal layer.

Edema in the dermis was a constant observation (figs. 4, 5, 6 and 7). The only specimen which did not show it was from a patient who was undergoing a winter remission. Dilatation of the blood vessels and lymph spaces was conspicuous. Interesting observations in five of the specimens were small focal areas of extravasation of red cells into the tissue sur-

rounding the blood vessels. In fourteen of the fifteen biopsy specimens a moderate to dense perivascular cellular infiltrate was present. In six the infiltrate was made up largely of lymphocytes and epithelioid cells, but in eight, in addition to the lymphocytes and epithelioid cells, eosinophils were numerous, and plasma cells were also present in three. The one specimen in which there was a striking absence of cellular infiltrate was taken during the winter, when the patient was undergoing a spontaneous remission. Numerous chromatophores in the upper part

Fig. 5.—Skin of the neck, after treatment, specimen from the same patient as that in figure 4. The dermis shows edema, and the blood vessels and lymph spaces are dilated. The cellular infiltrate in the dermis is decreased in amount.

of the dermis were noted in only two specimens. In all specimens the collagen and elastic tissue of the dermis showed basophilic degeneration, and in some this change was quite extensive. The ages of the 15 patients from whom these specimens were obtained ranged from 30 to 59 years. Their average age was 47 years. The degree of basophilic degeneration in most of the specimens was greater than would ordinarily be found in patients of the same age group.

Dopa reaction tests were done on two specimens from each of 2 patients who presented plaquelike lesions. On each patient one specimen was from an area which on clinical examination appeared to be depigmented. However, the dopa reaction showed essentially the normal number and arrangement of melanoblasts in the basal layer of all four biopsy specimens.

Specimens were obtained before treatment from 9 patients who presented lesions of the erythema solare perstans type. Histologically these specimens presented a picture somewhat similar to that found in

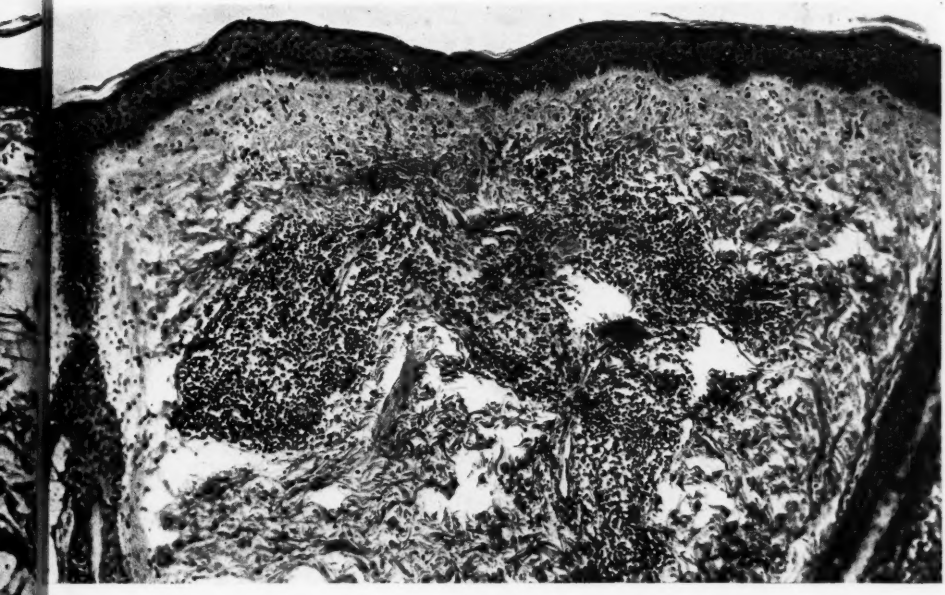

Fig. 6.—Polymorphic light-sensitive eruption, erythema solare perstans type, of skin of the neck. A relatively dense lymphocytic infiltrate is present in the dermis.

the plaquelike type of lesions. In seven the epidermis was atrophic. There was relative hyperkeratosis, and the hair follicles were plugged with keratin. Edema in both epidermis and dermis was conspicuous, but liquefaction degeneration of the basal layer was present in only three instances. Dilatation of the blood vessels was present in all these specimens, and on the whole a denser perivascular cellular infiltrate was seen in these specimens than in those from plaquelike lesions. Basophilic degeneration of the collagen and elastic tissue, which was present in all but 2 cases, was not as extensive as in the preceding group. The average age of this group of patients was 41 years, and the basophilic change was greater than is usually found at this age.

Four biopsy specimens were obtained before treatment from patients who presented contact eczematous type of lesions. Histologically these lesions differed from the other types of lesions found in polymorphic light-sensitive eruptions and more closely resembled those of eczema. The epidermis was acanthotic, and the stratum corneum showed areas of alternate hyperkeratosis and parakeratosis. There was pronounced intercellular and intracellular edema in the epidermis, which had progressed to spongiosis in at least 1 case. The dermis was also edematous, and blood vessels were dilated. A perivascular cellular infiltrate was present in all four specimens. Although lymphocytes and epithelioid

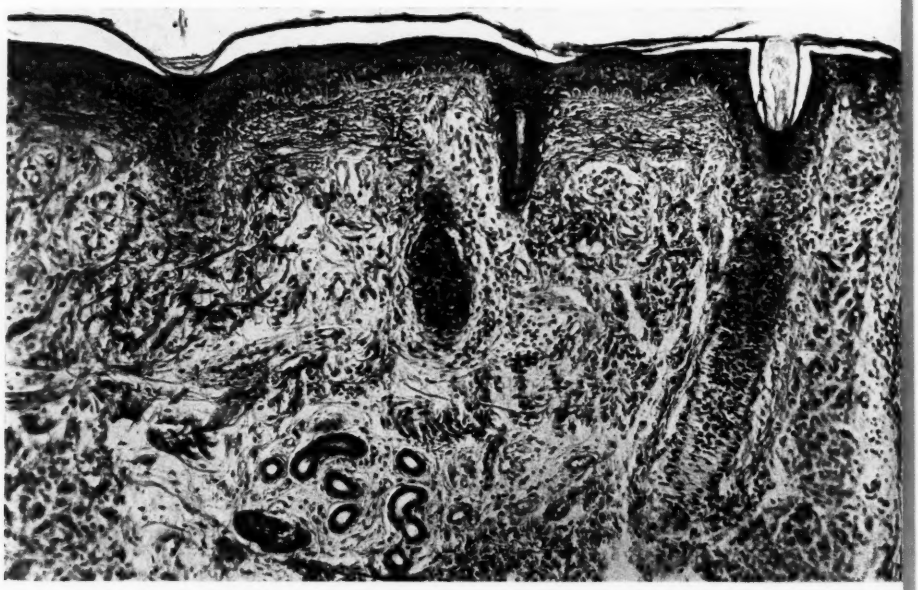

Fig. 7.—Skin of the neck after treatment, specimen from the same patient as that in figure 6. The cellular infiltrate in the dermis is slight.

cells predominated in the infiltrate in every case, eosinophils were present in notable numbers in three specimens, and plasma cells in three. Minute hemorrhages were found about some vessels in two of the biopsy specimens. In 1 case pigment in the basal cell layer of the epidermis was conspicuous and numerous chromatophores were present in the dermis. The patients in this group, whose average age was 42 years, did not show the extensive basophilic degeneration of the collagen and elastic tissue seen in the other two groups of patients.

No biopsy specimen was obtained before treatment in the patient who presented the papular prurigo type of lesions.

PHYTOPHOTODERMATITIS

Since there are numerous reports in the literature (Gross and Robinson,[22] Oppenheim,[23] Cummer and Dexter [24] and Sams [25]) of the role of plants and foods in photosensitization, it was felt that these factors should be considered in solar dermatitis.

On the assumption that solar sensitivity might possibly be caused by some contacted external agent plus sunshine, 25 selected persons (farmers and oil field workers) with localized eczematous solar dermatitis were given patch tests to the oleoresins of sixty common Texas weeds and other known environmental contactants such as crude oil, tractor oils and greases and soaps. Samples were placed on the back and allowed to dry, and the test sites were then exposed to the midday sun for fifteen minutes. Test sites were observed at intervals for seventy-two hours. Since no positive reactions were observed, it was concluded that these external environmental contactants probably played no part in the causation of the solar sensitivity in these cases.

An additional 15 patients with solar dermatitis were tested on the back with twenty-five ether extracts of common Oklahoma weeds. All tests were observed at twenty-four, forty-eight and seventy-two hours. Only 1 patient, a woman with vesicular contact type solar dermatitis of thirty years' duration, showed a positive reaction to marsh elder. At the same time these patients were treated on the back with ultraviolet radiation from a Fisher cold quartz lamp. A 4 inch (10 cm.) area was tested at an 8 inch (20 cm.) distance, with a fifteen second exposure. In all the cases there was an erythema in twenty-four hours. Five of the patients exhibited pronounced erythema even with five seconds' exposure and seemed to have a hypersensitivity to sunlight or, as Epstein suggested, a pathologic sunburn reaction. None of these patients had eczema at the site of the erythema. At the same time, they were tested to the Wood light for one minute, at a 4 inch distance. No positive reactions were elicited. The same patients in whom the weed tests were negative were given ultraviolet (cold quartz) radiation through the twenty-five

22. Gross, P., and Robinson, L. B.: Berlock Dermatitis: Unusual Dermatitis and Pigmentation Following Use of Perfume, Arch. Dermat. & Syph. **21**:637, (April) 1930.

23. Oppenheim, M.: Beitrag zur Ätiologie der Dermatitis striata pratensis bullosa, Wien. med. Wchnschr. **86**:1276, 1936; cited by Stokes, Beerman and Ingraham: Am. J. M. Sc. **203**:608, 1942.

24. Cummer, C. L., and Dexter, R.: Dermatitis Caused by Dictamnus Albus (Gas Plant): Example of Photosensitization, J. A. M. A. **109**:495 (Aug. 14) 1937.

25. Sams, W. M.: Photodynamic Action of Lime Oil (Citrus Aurantifolia), Arch. Dermat. & Syph. **44**:571 (Oct.) 1941.

26. Footnote deleted.

round apertures in the cardboard used in the weed tests, to the areas to which the weed oils had been again applied and on which they had been allowed to dry. They all acquired erythema as seen on previous test sites to sunlight, but none of them manifested an eczematous, vesicular or squamous type of eczema. These experiments failed to show that these weeds exhibit any photosensitizing properties under the conditions noted.

Six patients were tested with two minute exposure to cold quartz light over an area 4 inches in diameter on the back. All tests resulted in pronounced erythema, purplish and without vesiculation. One patient (figs. 8 and 9) with the contact type of solar dermatitis showed in seventy-two hours an extensive exacerbation of the previous lesions,

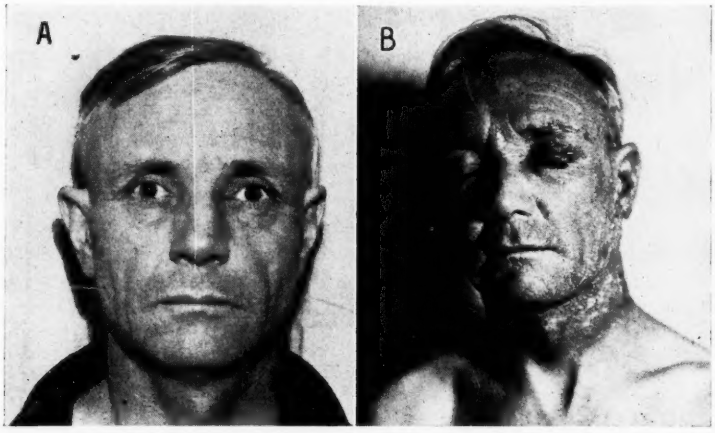

Fig. 8.—Exacerbation of solar eczema in all previously involved areas produced by four minutes of ultraviolet radiation from a cold quartz lamp to a 3.5 cm. aperture at 12 inches (30 cm.) distance on the back. The condition is now in remission with administration of gonadotropin and testosterone. *A*, the patient as observed before ultraviolet irradiation. *B*, the patient forty-eight hours after irradiation.

with pathologic sunburn reaction on the tested site. A similar reaction was described by Sellei and Liebner [27] and Epstein.

Considering the possibility that ingested foods might act as sensitizers to sunlight an additional 25 patients with solar dermatitis were given patch tests with the ether extract of sixty common vegetables, fruits and grains. The extracts to be tested were placed on the back, and the test sites were covered with a "band-aid" to exclude light. Test sites were examined at twenty-four, forty-eight and seventy-two hour intervals. No positive reactions were elicited.

27. Sellei, J., and Liebner, E.: Ueber Prurigo aestivalis, Arch. f. dermat. u. Syph. **152**:19, 1926.

At a later interval all 25 patients were retested with the sixty food extracts but the test sites were not covered. As soon as the test sites were dry the patients were exposed to the midday sun for fifteen minutes. Test sites were observed for twenty-four, forty-eight and seventy-two hours. Five patients gave 1 + to 4 + reactions to parsnip, and 4 of the same patients gave similar reactions to parsley. Both these plants belong

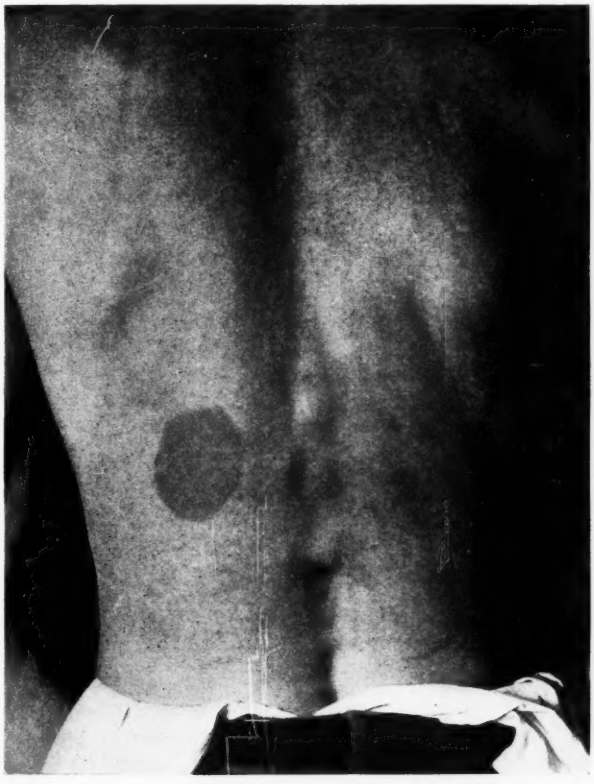

Fig. 9.—Pathologic sunburn reaction without vesiculation produced on the back by the exposure described in the legend for figure 8.

to the carrot family, long known to contain photosensitizing agents. None of these patients admitted eating either parsnip or parsley. The sixth reactor gave a 4 + reaction (vesiculation) to eggplant and had erythema at the site of the potato test. This patient stated that he did not eat eggplant, and the removal of potato from the diet did not influence the eruption. In the remaining 19 patients all test sites showed no reactions. In addition, fairly carefully controlled elimination diets failed to bring

about an improvement of symptoms in any of these persons. Similarly, ingested drugs could be eliminated as a causative factor in these cases.

SUMMARY OF LABORATORY DATA

Routine blood examinations for 14 of the patients reported in this series showed essentially normal conditions. The average white cell count was 7,785; the average total red cell count was 4,630,000, and the average proportion of hemoglobin was 91 per cent. In 5 patients in the acute stage of the disease total serum protein values and albumin-globulin ratios were within normal limits.

The question of porphyrins as a causative agent in photosensitization was considered. Urinary porphyrin determinations were carried out on 15 patients. Five had the acute stage of the disease; in 6 the condition was in moderate remission, and 4 patients were experiencing complete winter remission. In several instances more than one determination was done. Results for all 15 patients revealed no uroporphyrin or porphobilinogen.

Base line studies with reference to urinary creatine and 17-ketosteroid excretion were obtained on 31 men and on 3 women with solar dermatitis. Over a period of three years, in 5 men and 1 woman, studies were carried out during periods of hormonal therapy with equine gonadotropin [28] and testosterone propionate.

Four men and 1 woman were treated with testosterone propionate. Twenty-four hour urine collections were used for all determinations. Determination of creatine-creatinine excretion was done by the method of Folin. Twenty-four hour excretion of urinary 17-ketosteroids was determined by the method of Robbie and Gibson.[29] In all but four instances two consecutive determinations were done to establish the base line figures. The treatment with equine gonadotropin for the 6 patients has been over periods ranging from four months to one year. In 4 patients results were excellent. In 2 instances moderate improvement was observed. Of 4 patients receiving testosterone propionate, 2 showed excellent response and in 2 others the response was equivocal. The observations are presented in table 2.

The initial values for urinary creatines in men averaged 115.27 mg. in twenty-four hours, approximately 100 mg. above normal. Normal creatine excretion was present in 5 of the men. Excretion levels ranged from 0.0 mg. in 5 instances to over 200 mg. in twenty-four hours in the

28. The following contributions of material for use in these experiments were made: equine gonadotropin (anteron®) and testosterone propionate (oreton®) by the Schering Corporation, equine gonadotropin (gonadogen®) by the Upjohn Company and equine gonadotropin (antex®) by Ayerst, McKenna and Harrison.

29. Robbie, W. A., and Gibson, R. B.: Rapid Clinical Determination of Urinary 17-Ketosteroids, J. Clin. Endocrinol. **3**:200, 1943.

other patients. Higher levels were observed in the 2 women. The degree of creatinuria could be correlated with the intensity of the cutaneous lesions. This physiologic expression of the disease was found to be significantly influenced by administration of both gonadotropin and testosterone propionate in both sexes.

Normal values for 17-ketosteroid excretion were encountered nine times in the initial studies of the 31 men. Average excretion of 17-ketosteroids was found to be 9.5 mg. in twenty-four hours in the men

TABLE 2.—*Average Creatine-Creatinine and 17-Ketosteroid Excretion in Solar Dermatitis*

	No. of Patients	Average Age	Average Age at Onset	Average Total Creatinine, Mg./24 Hr.	Average Preformed Creatinine, Mg./24 Hr.	Average Creatine, Mg./24 Hr.	Average 17-Keto-steroids, Mg./24 Hr.
				No Treatment			
Men	31	46	42	1,538.49	1,123.21	115.27	9.5
Women	3	45.3	19.3	1,490.58	1,115.53	312.04	11.4
				Equine Gonadotropin Therapy			
Men	5	40.5	37.5	1,678.10	1,620.50	57.57	11.4
Women	1	46	13	1,217.29	995.85	221.97	8.2
				Testosterone Propionate Therapy			
Men	4	50.2	42.5	1,314.09	1,253.65	60.43	8.0
Women	1	49	42	1,340.34	997.20	343.26	9.0
				Normal Values			
Men	..	....	....	individual	.....	< 20	8-20
Women	..	....	....	variation (k)	.....	± 50	5-15

TABLE 3.—*Seminal Studies in Solar Dermatitis*

	No. of Patients	No. of Studies	Average Age	Average Volume, Ml.	Average Motility, %	Average No. of Sperm Cells/Ml.	Average Total No. of Sperm Cells
No treatment	16	17	41.2	3.50	46.3	48,538,625	199,991,637
Equine gonadotropin therapy	4	11	39	2.36	51.8	38,909,090	100,413,636
Testosterone propionate therapy	1	1	49	1.1	1.0	1,400,000	1,540,000
Normal values [30]	..	..	....	4.0	> 80	120,650,000	.....

and 11.4 mg. in twenty-four hours in the women. Since the average excretion was barely within the lower limits of normal for adult males and there is normally a daily variation of several milligrams, values above 10 mg. in twenty-four hours are taken as above the low normal. Therefore, the average of 9.5 mg. in twenty-four hours may be interpreted as low normal. Prior to and after treatment the figures on the 3 women were well within normal range.

Considerable difficulty was encountered in securing seminal specimens collected under conditions acceptable for laboratory evaluation. However, adequate initial studies have been carried out on 16 patients. The average age of these men was 46.3 years. Observations on these patients are shown in table 3.

Three men had sperm counts above the lowest number compatible with fertility. The other 13 patients showed moderate to severe oligospermia with 1 instance of azoospermia. Since seminal adequacy is evaluated on volume of ejaculate, motility of cells and number of cells per milliliter as well as on total number of cells and other factors,[30] the over-all evaluation of seminal adequacy for this group is seen to be low.

TREATMENT

Systemic treatment in light-sensitive eruptions has been largely confined to the use of gold and sodium thiosulfate. A limited number of patients with solar dermatitis respond to gold therapy temporarily, but this form of therapy is not too satisfactory.

Physical means of filtering the exciting wavelengths are widely employed in the form of lotions and ointments. Such filters include salicylates, quinine or tannic acid. More recently paraaminobenzoic acid and its esters have been successfully employed by Rothman [31] and others. However, side reactions of an allergic nature in patients were reported by Baer and Meltzer [32] and in a patient seen by one of us (J. H. L.) have imposed limitation of the use of paraaminobenzoic acid clinically. A 5 per cent preparation of menthyl anthranilate (a substance related to paraaminobenzoic acid) and titanium dioxide in a vanishing cream base [33] has been employed as a filter for 30 patients with a variety of other actinic dermatoses (farmers' and sailors' skin, for example) with most satisfactory results under conditions of severe exposure. No side reactions were experienced by any of these patients.

Among the antihistaminic group of compounds, tripelennamine (pyribenzamine®) was shown to exert its effect by acting as a filter, rather than as an antihistaminic, by Baer, Kline and Rubin.[34] However, Rothman [35] interpreted Baer's observations on the basis of the definite antihistaminic action of tripelennamine. Tyson [36] reported that diphenhydramine (benadryl®) caused permanent relief of an urticarial response to sunlight associated with premenstrual exacerbations in a female Negro.

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30. Hotchkiss, R. S.; Brunner, E. K., and Grenley, P.: Semen Analysis of 200 Fertile Men, Am. J. M. Sc. **196**:362, 1938.

31. Rothman, S., and Henningsen, A. B.: The Sunburn Protecting Effect of Para-Amino-Benzoic Acid, J. Invest. Dermat. **9**:307, 1947.

32. Baer, R. L., and Meltzer, L.: Sensitization to Mono-Glycerol Para-Amino Benzoate, J. Invest. Dermat. **11**:5, 1948.

33. A-fil® was supplied for these studies by the Texas Pharmacal Company, San Antonio, Texas.

34. Baer, R. L.; Kline, P. R., and Rubin, L.: Nature of Inhibition of Ultraviolet Erythema by Pyribenzamine, J. Invest. Dermat. **11**:405, 1948.

35. Rothman, S., in discussion on Baer, Kline and Rubin.[34]

36. Tyson, W. G.: Hypersensitiveness to Sunlight and Dysmenorrhea Controlled by Benadryl, J. Invest. Dermat. **7**:209, 1946.

Urbach [37] suggested the importance of a dietary regimen in treatment of actinic dermatoses. He also stressed the importance of bacterial toxins and reported a case of hypersensitivity to light in which a cure was effected by cholecystectomy. It is questionable, as yet, whether phenindamine (thephorin®) ointment may act in any way as a filter, but its anesthetic effect is of value in the relief of pruritus.

The efficacy of estrogens in treatment of sunlight eruptions has been reported by Selisky,[38] Goldberg,[39] Lancaster,[40] Hadley,[41] Epstein [17] and

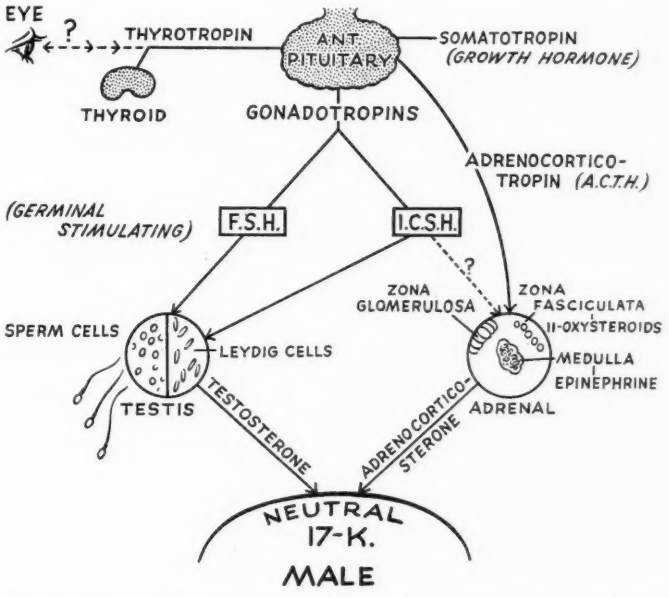

Fig. 10.—Diagram showing relation of gonadotropic and adrenotropic hormones to the gonads and the adrenal glands in the male. (The influence of light on the pituitary gland in human beings is still questionable.)

Lain and associates,[20] and interpretation of results is difficult, since in many instances the patient presented menopausal symptomatology.

37. Urbach, E., and LeWinn, E. B.: Skin Diseases, Nutrition and Metabolism, New York, Grune & Stratton, Inc., 1946, p. 514.

38. Selisky, A. B.: Neue Behandlungsmethode von Lichtdermatosen, Klin. Wchnschr. **101**:1299, 1935.

39. Goldberg, M. A.: Climacteric Hypersensitiveness to Light and Effort: Treatment with Follicular Hormone (Theelin), J. Allergy **6**:298, 1935.

40. Lancaster, A. H.: Estrogenic Hormone Therapy in Sunlight Eruptions of the Female, South. M. J. **32**:495, 1939.

41. Hadley, H.: Urticaria Solaris, Urol. & Cutan. Rev. **45**:406, 1941.

Hormonal therapy has been used in a limited number of cases. The rationale for substitution of exogenous steroids or stimulation of production of endogenous steroids has been on the basis of laboratory data which indicate nitrogen loss in these patients. Thus far, the treatment is promising.

One or more biopsy specimens were obtained from patients after hormone treatment. Two of these persons had received testosterone propionate (oreton®), and 5 had received equine gonadotropin (either anteron® or gonadogen®). In all but one of these specimens the most striking finding was a significant decrease in the amount of the perivascular cellular infiltrate. Three showed less edema in the epidermis, and four, less edema in the dermis. In two that had shown minute hemorrhage about blood vessels before treatment, no evidence of extravasation of red cells was found after treatment. Although the number of specimens after treatment that have been examined is too small to warrant any definite conclusions, they indicate that there are some microscopic morphologic changes to support the clinical impression of improvement following hormone therapy.

COMMENTS

Previous attempts to clarify the classification of Haxthausen's group of chronic polymorphic light-sensitive eruptions have been unsuccessful. He included in this group prurigo aestivalis, eczema solare and summer acne. The variability of the lesions renders classification difficult, but morphology seems to be the best basis for classification when one studies the problem as a whole.

With the demonstration of porphyrins in several cases of eczema solare by Goeckerman and his associates [21] and by Templeton and Lunsford,[42] a classification of this group on the basis of porphyrin studies seemed promising. However, Blum,[43] Turner and Obermayer,[13] Brunsting [44] and others found little evidence to prove that the porphyrins are related to photosensitivity in man.

Another possible basis of classification was the active wavelength which produces each type of lesion, but reports of such studies are few and conflicting. Schaumann and Lindholm [45] and Blum [46] showed that

42. Templeton, H. J., and Lunsford, C. J.: Eczema Solare and Porphyria, Arch. Dermat. & Syph. **25**:691 (April) 1932.

43. Blum,[16] p. 237.

44. Brunsting, L. A.: Porphyria with Cutaneous Manifestations, Proc. Staff Meet., Mayo Clin. **22**:489, 1947.

45. Schaumann, J., and Lindholm, F.: Études cliniques, actinobiologiques et histologiques sûr le summer-prurigo d'Hutchinson, Ann. Inst. d'actinol. **6**:93, 1932.

46. Blum,[16] p. 242.

their patients reacted to the sunburn spectrum, while Urbach and Konrad [47] found their patient to be sensitive to the blue and violet spectrum.

Epstein [17] was able to demonstrate three different types of sensitivity to light—immediate urticaria (whealing reaction), pathologic sunburn reaction and specific lesions of prurigo, chronic type—in reporting cases of solar dermatitis. Seven were combinations and transitional forms of the urticarial, prurigo-like and eczematous types of solar dermatitis; 8 were prurigo aestivalis, and 2 were eczema solare.

These manifestations of sensitivity to light seemed independent of each other, and they corresponded essentially to the clinical entities of urticaria solare, eczema solare and prurigo aestivalis. The three forms of sensitivity to light were not due to specific wavelengths, for each one of them had been effected by more than one spectral region. Prurigo-like lesions were provoked experimentally in a patient who had a normal reaction to sunburn radiation. Therefore, this phenomenon was not dependent on the sunburn wavelength. Thus, the activating wavelength is not as yet a means of classifying the chronic polymorphic light-sensitive eruptions.

When one sees a great number of these patients, a descriptive term such as "chronic polymorphic light eruption" seems rather vague and does not define the type of lesions seen. All these lesions may be categorically placed in one general group as polymorphic eruptions due to light, but the majority of our patients fall into fairly definite groups in which certain types of lesions predominate.

Two of the four types seen are more definite clinical entities and are more easily recognized than the others. The plaquelike type is the most clearly defined type of lesion encountered (in 65 per cent of the 34 patients seen in Oklahoma City, and in approximately 75 per cent of the remaining 145 studied in Texas). The thickened, indurated plaque which cannot be shown by photography but must be identified by palpation is diagnostic. Whether this group represents an advanced stage of erythema solare perstans or the erythema multiforme–like type has not been proved.

The contact eczematous type of lesion characterizes another definite group. Dermatologists usually make a diagnosis of contact eczema on most of the patients with this form of eruption, and routine patch tests give negative results. It is in this type that the photodynamic action of drugs, bacteria, weeds and ingested food (parsnip and soy beans, for example) should be considered. The studies reported here offer no positive proof of an etiology of this nature.

47. Urbach, E., and Konrad, J.: Ueber eine durch den langwelligen Anteil des Sonnenspectrums erzeugte Lichtdermatose von Typus der Prurigo aestivalis Hutchinson, Strahlentherapie **32**:193, 1929.

The papular prurigo eruption was infrequently seen in our 34 investigated cases. Pruriginous lesions were associated with the other forms of sunlight eruptions in many patients. Prurigo aestivale is a term used loosely for all sunlight eruptions and should be reserved for those in which the pruriginous lesions predominate.

The last type, the erythema multiforme–like eruption or erythema solare perstans, is the most difficult one to differentiate from lupus erythematosus. It is felt that some patients exhibiting this type of lesion may have borderline cases of lupus erythematosus. Many of these patients respond well to gold and sodium thiosulfate therapy, which observation could possibly be further proof of close similarity of this type to a photosensitive form of lupus erythematosus.

Although the microscopic picture in polymorphic light-sensitive eruptions is not specific, the study of the histopathology of these lesions reveals some interesting facts. For example, the contact eczematous type shows changes resembling those found in eczema. The fact that the contact eczematous type could be separated both clinically and histologically was of interest to us. The microscopic differences between the plaquelike type and the erythema solare type are not so definite. Differentiation of these types from lupus erythematosus is also difficult in some cases.

Hausmann and Haxthausen [2] were probably the first to suggest that in solar dermatitis the initial injury is to the epidermal cells, with release of a vasodilator substance which, through diffusion, brings about changes in the blood vessels and edema in the dermis. The biopsy specimens in this series showed no changes in the epidermal cells other than intracellular and intercellular edema. However, a chemical reaction, such as that postulated by Hausmann and Haxthausen, might produce no morphologically demonstrable change.

Further work is indicated on the physiology of pigment in this disease. There are areas which appear depigmented on gross inspection, and melanin in the basal layer seems to be rather spottily distributed in sections stained with hematoxylin and eosin. However, dopa reaction testing on two lesions which were thought on gross inspection to be depigmented showed an essentially normal distribution of melanoblasts. Although the number of dopa reaction tests done is too small for one to draw any definite conclusions, the results suggest that, if there is any disturbance in pigment formation, it occurs in the conversion of the precursor to melanin and not in an absence of melanoblasts.

Changes in the elastic tissue and the collagen of the dermis in patients with solar dermatitis have been mentioned by Hausmann and Haxthausen,[2] Piers [48] and others. These changes are essentially the ones

48. Piers, F.: Sunlight and Skin Cancer in Kenya, Brit. J. Dermat. & Syph. **60**:319, 1948.

which occur in the skin with advancing age. The biopsy specimens in the series reported here from the plaquelike and erythematous types of lesions showed more extensive degenerative changes than would be expected in normal persons of the same age. However, whether these changes represent a cause or an effect of these lesions produced by sunlight is still questionable.

Since it is sometimes difficult to differentiate lesions of polymorphic light-sensitive eruptions from those of lupus erythematosus, it is of interest that the results of routine blood studies on the patients reported here were normal. In 5 patients with the acute stage of the disease, serum protein values and albumin-globulin ratios were within normal limits.

Numerous authors have reported that photosensitization (geeldikkop) may be evoked in animals by the ingestion of certain plants, notably Tribulus terrestris. The work of Rimington and Quinn [49] demonstrated that this plant induced photosensitization associated with the presence of a porphyrin (phylloerythrin). The absence of sensitivity to food as a causative agent in these patients with solar dermatitis may perhaps be correlated with negative results of tests for urinary porphyrins which were carried out on 15 of the 31 light-sensitive men. The probability of photosensitization in solar dermatitis caused by food and/or porphyrin is therefore remote.

A possible explanation of the etiology of solar eczema on the basis of physical allergy is suggested by the fact that in a few of the patients an immune reaction to sunlight was observed. After the initial exposure in the spring to sunlight, a severe exacerbation of the lesions occurred, but later in the summer only mild responses were evoked. Hutchinson [50] suggested that in some instances heat radiation was the causative agent, since the lesions may not be restricted entirely to exposed areas of the skin. Blum [51] expressed the belief that the lesions of solar eczema are abnormal responses to light radiation which are qualitatively different from those of normal sunburn. He concluded that "the complexity of the problem is not lessened by the possibility that radiation from other regions of the spectrum may, in some cases, produce clinical pictures similar to those brought about by sunburn radiation, although the

49. Rimington, C., and Quinn, J. I.: The Biological Formation of Phylloerythrin in the Digestive Tract of Various Domesticated Animals, J. South Africa Vet. M. A. **8**:141, 1937. Quinn, J. I.; Rimington, C., and Roets, G. C. A.: Thick Head or Yellow Head Disease During Grazing in Pasture, Onderstep'oort J. Vet. Sc. & Animal Indust. **4**:463, 1935. Quinn, J. I.: Comparative Reaction of Merino Sheep Following Continued Exposure to Sunlight and Shade, South African J. Sc. **43**:252, 1947.

50. Hutchinson, J.: Summer Prurigo, in Lectures on Clinical Surgery, London, J. & A. Churchill, 1878, vol. 1, p. 126.

51. Blum,[16] p. 250.

etiology must obviously be quite different." On the basis of our clinical observations it is evident that heat cannot be excluded as a possible factor in these cases.

Apparently chronic or acute solar dermatitis, as well as other dermatologic disorders, results in creatinuria. While the observation is nonspecific, it represents metabolic derangement with reference to proteins and may be controlled by administration of testosterone propionate or by indirect stimulation of endogenous androgen production. The 4 patients who were treated with testosterone propionate showed subsequent amelioration or total absence of creatinuria. Stimulation of the testis to produce endogenous androgen by daily administration of gonadotropin from pregnant mare's serum, 500 to 1,000 international units daily, resulted in more rapid and sustained improvement, and the systemic response was pronounced.

Tanning of the skin has been observed, and while the role of androgens in this process is not completely understood as yet, they do enter into the physiology of melanin production; in the presence of depressed androgen production melanin is absent.[52] Stokes, Beerman and Ingraham [53] reiterated the role of the sex steroids in tanning of the skin.

Since 17-ketosteroids are for the most part of adrenal origin, the possibility of moderate adrenal depression should be considered in terms of the general adaptation syndrome of Selye.[54] The known response of the adrenal gland to any bodily insult [55] is the probable explanation for the average excretion of 9.5 mg. in twenty-four hours, and this response in turn would of course affect nitrogen metabolism. As yet, there is no proof as observed on biopsy that the testicular Leydig tissue is changed in these patients with the treatment.

Since the androgenic and spermatogenic functions of the testis are controlled by two different pituitary hormones (fig. 7), the seminal deficiency observed in a small number of the men probably must be explained on a separate basis. Impairment of seminal function unaccompanied by androgenic failure is far more frequent than was once thought.

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52. Edwards, E. A.; Hamilton, J. B.; Duntly, S. C., and Hubert, G.: Cutaneous Vascular and Pigmentary Changes in Castrate and Eunuchoid Men, Endocrinology **28**:119, 1941.

53. Stokes, J. H.; Beerman, H., and Ingraham, N. R.: Photodynamic Effects in Dermatology, Am. J. M. Sc. **203**:608, 1942.

54. Selye, H.: The General Adaptation Syndrome and Diseases of Adaptation, in Textbook of Endocrinology, Acta Endocrinologia, Université de Montreál, Canada, 1947, p. 837.

55. Forbes, A. P.; Donaldson, E. C.; Reifenstein, E. C., Jr. and Albright, F.: Effect of Trauma and Disease on the Urinary 17-Ketosteroid Excretion in Man, J. Clin. Endocrinol. **7**:264, 1947.

Several factors must be considered as causative agents in seminal insufficiency: (1) extraendocrine factors, such as diet, disease of the adrenal gland or the thyroid and other diseases, including infections or fevers; (2) primary failure of the germinal epithelium; (3) moderate failure of the gonadotropin from the anterior lobe of the pituitary gland.

In these patients, low grade adrenal depression may possibly be an adjuvant of the seminal inadequacy. As far as the pituitary gland is concerned in solar dermatitis, assays for depressed pituitary function have been done in only 2 instances. The titers for pituitary gonadotropin were not elevated. It is, however, known that cyclic changes in spermatogenesis and androgen production may be caused to appear out of season in animals (birds, and ferrets of both sexes) that have cyclic breeding seasons by means of prolonged exposure to light. That the effect is mediated by the pituitary body has been amply demonstrated by Benoit,[56] Bissonnette [57] and others.

Nevertheless, there still is no evidence that sunlight has any effect on androgen production and maturation of germ cells as mediated through the pituitary gland in the human male. All that can be said is that sunlight influences the pituitary gland.

It has been shown by many clinical reports that there is at this time no satisfactory treatment, hormonal or otherwise, for intrinsic testicular failure. Hence, the essentially unchanged status of the germinal epithelium, as far as the seminal findings reported here are concerned, is not surprising.

CONCLUSIONS

A classification of polymorphic light-sensitive eruptions based on morphologically and clinically demonstrable variations is suggested.

Histologic examination showed nonspecific inflammatory changes, edema in both the epidermis and the dermis and a cellular infiltrate about dilated blood vessels in the corium. These changes were less pronounced during winter remissions and after hormone therapy.

Photosensitivity on an allergic basis from foods and weeds may be ruled out in most cases of solar dermatitis.

The absence of porphyrins in the urine of all patients tested for them eliminates these substances as photosensitizing agents in solar dermatitis.

The creatinuria and moderately depressed 17-ketosteroid excretion may be ameliorated by the administration of testosterone propionate or by

56. Benoit, J.: Facteurs externes et internes de l'activité sexuelle: I. Stimulation par la luminière de l'activité sexuelle chez le canard et la cane domestiques, Bull. biol. France et de la Belgique **70**:487, 1936.

57. Bissonnette, T. H.: Sexual Photoperiodicity, Quart. Rev. Biol. **11**:371, 1936. Bissonnette, T. H., and Bailey, E. E.: Litters from Ferrets in January Induced by Increased Exposure to Light After Night-Fall, Am. Naturalist **70**:454, 1936.

stimulation of endogenous androgen production in men by the administration of equine gonadotropins with resultant clinical remission observed for most patients.

ABSTRACT OF DISCUSSION

Dr. William H. Goeckerman, Los Angeles: I am not sure that I can adequately discuss the paper by Drs. Lamb and Shelmire, because their experience with solar dermatitis is evidently unique. While we have all seen the variety of morphologic characteristics of solar dermatitis they describe, their material is unusual. While there are many sun worshippers in southern California, it is only occasionally one sees real chronic dermatitis. Most of these persons know they are sensitive and have been in a position to protect themselves. One would suspect that meteorologic or ethnic conditions might have been a factor in the authors' series. I have always looked on the chronic plaquelike condition as secondary to irritation or scratching, a modified form of lichenification. Through the years I can recall only 2 or 3 cases that proved difficult of differentiation from true lupus erythematosus.

Dr. George C. Andrews, New York: This is an interesting subject, and I am thankful to Dr. Lamb for the way he covered it. He called attention to things that are still rather new to us. I should like to mention a case of a yacht designer who for over twenty years had had a breaking out of nodules on his temples, face and neck when he was exposed to sunlight. These nodules were clinically very similar to sarcoid. Histologically, Dr. Machacek reported them as lymphosarcoma with a possible alternate diagnosis of a deep type of lupus erythematosus. These nodules would appear a day or two after exposure to sunlight, remain for two or three weeks and disappear without leaving any sign. This was a very unusual solar dermatitis, which might be called a lymphocytomatous type. Another patient we saw recently was a child of 8 who had had summer prurigo for five or six years. This patient had a thorough work-up and showed a rather high creatinine excretion; the child is under treatment now with female hormones in amounts suggested by Dr. Lamb. There is just one other thing I want to mention, and that is a case encountered by Dr. James Hamilton, professor of anatomy at Long Island College of Medicine, of a boy who had a tumor of the testes. The patient had had both testicles removed at the age of 8. He had never tanned and was the fair blond type. At the age of 14 he was exposed to sunlight while clad in bathing trunks. A week after exposure to sunlight he was given an injection of testosterone for the first time. The area exposed to the sunlight became heavily pigmented. This observation shows, the decided effect of hormones on the pigments of the skin and on sensitization to light.

Dr. F. R. Schmidt, Chicago: Dr. Lamb, in his classification of solar dermatitis, referred to the occurrence of sharply demarcated plaques of erythema on the face. This type has not previously been stressed in discussions on this subject, and we are indebted to Dr. Lamb for calling our attention to it. I, too, have observed these plaques and noticed that they often do not disappear. Their persistence is understandable when one remembers that sunlight not only destroys material in the skin necessary for normal function, such as riboflavin, but may liberate histamine, which in turn damages the small blood vessels and leads to permanent abnormalities in the local circulation.

DR. MARION B. SULZBERGER, New York: I wonder whether Dr. Lamb would tell us something in more detail about the hormone therapy he and his associates would recommend.

DR. JOHN H. LAMB, Oklahoma City: In answer to the question about therapy, we use gonadotropic hormone from pregnant mares' serum (anteron® and gonadogen®). We gave approximately 500 to 1,000 international units daily or every other day, as was possible, and, contrary to Dr. Shelmire's remarks, we have seen some dramatic effects, particularly in those below 50. It happened that several of the patients whom Dr. Shelmire saw were the older men past 50 years of age who did not receive any benefit from administration of equine gonadotropin. The theory behind this occurrence is that in those past 50 the Leydig cells of the testes are slower in their response to any stimulus from the pituitary body. In the younger men the Leydig cells still respond fairly well to the gonadotropic stimulus from the pituitary gland artificially produced by the gonadotropic hormone.

Dr. Andrews's description of the sarcoid-like case of light-sensitive eruption was very interesting. In 2 of our severe cases of the plaquelike eruption the infiltrate was suggestive of mycosis fungoides.

In closing I wish to stress one point again, that is, the effect of fluorescent lighting on light-sensitive eruptions. In 5 cases clinical evidence pointed toward the fact that this form of light is capable of both provoking and prolonging the eruption. However, further laboratory study must be done on this problem.

URTICARIA PIGMENTOSA (LARGE NODULAR TYPE)

Report of a Case

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URTICARIA pigmentosa of the large nodular type is of sufficient rarity to cause diagnostic problems. The condition may remain undiagnosed unless a specimen is removed and examined microscopically after the tissue has been stained with one of the basic aniline dyes. Finnerud [1] and Little [2] in excellent reviews stated that in approximately 10 per cent of cases of urticaria pigmentosa the lesions are of the nodular type. However, the occurrence of large tumors in urticaria pigmentosa similar to those observed in our case is apparently unrecognized. We wish to report such a case and to comment briefly on the prognosis and the association of heparin with the mast cells.

REPORT OF A CASE

A 21 month old American boy of Syrian parentage was seen at the Mayo Clinic in November 1946. Since birth this patient had been normal except for brown oval and round nodules on the neck, extremities and trunk which were occasionally pruritic. Bullae had been noted on these nodules, but they had begun to disappear when the patient was 1 year old. For the past four months the nodules had been decreasing in size. There was no history of purpura or any hemorrhagic tendencies.

The family history was noncontributory. The patient had no siblings.

The examination of the skin revealed approximately twenty-five circumscribed oval brown to almost black elevated indurated plaques and nodules scattered over the trunk, neck and extremities (fig. 1). The primary lesion consisted of a nodule varying in diameter from 1 to 4 cm. and elevated up to 1 cm. above the surrounding skin. No bullae were present (fig. 1*c*). On stroking of the lesions no urtication occurred. The general examination gave essentially normal results. The clinical diagnosis rested between juvenile xanthomatosis, nevoxanthoendothelioma, myoblastoma and urticaria pigmentosa.

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*From the Section on Dermatology and Syphilology, Mayo Clinic.

1. Finnerud, C. W.: Urticaria Pigmentosa (Nodular Type) with a Summary of the Literature: Report of a Case, Arch. Dermat. & Syph. **8**:344-358 (Sept.) 1923.

2. Little, E. G.: A Contribution to the Study of Urticaria Pigmentosa, Brit. J. Dermat. **17**:355-373 (Oct.) 1905; **18**:16-38 (Jan.) 1906.

Normal conditions were noted on examination of the urine, blood count and roentgenograms of the thorax.

Tissue for histopathologic study was taken from the dorsum of the right hand and fixed in formaldehyde solution U. S. P. On examination of a specimen prepared by the frozen section method no intracellular or extracellular deposition of fat in the section was noted. The remainder of the tissue was embedded in paraffin and stained with hematoxylin and eosin, Van Gieson, elastin H, Maresch-Bielschowsky and polychrome methylene blue stains. The section showed a relative and absolute hyperkeratosis and a flattening of the rete pegs. A dense cellular

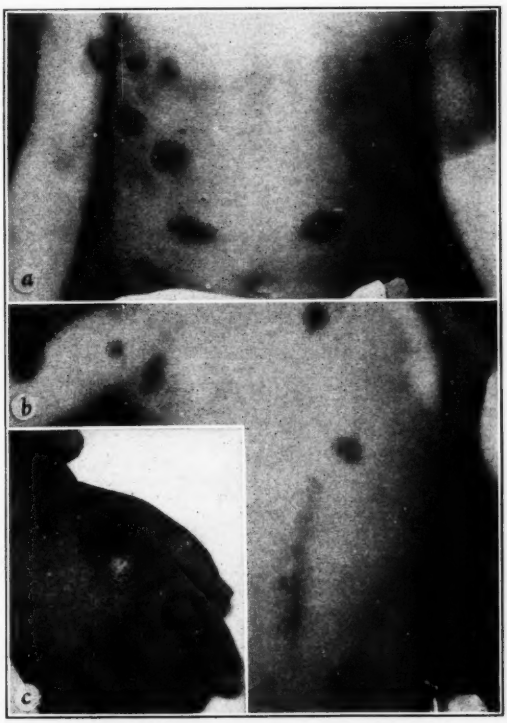

Fig. 1.—Urticaria pigmentosa: (*a*) anterior view; (*b*) posterior view; (*c*) large nodule over the dorsum of the right hand.

infiltrate consisting entirely of large granular cells arranged in columns occupied the corium. Since the polychrome methylene blue stain did not demonstrate the metachromatic granules of the mast cells the diagnosis of urticaria pigmentosa was dismissed. Furthermore, the slides were presented at a histopathologic conference and that diagnosis again discarded. Months later, at the suggestion of Dr. Fred Weidman,[3] additional recuts were stained by the Giemsa method and the meta-

3. Weidman, F., cited in personal communication from Hamilton Montgomery to the authors.

chromatic granules typical of mast cells were recognized. These granules stained purple by the Giemsa method, the nucleus and the cytoplasm staining blue. The majority of the mast cells were mononucleated; however, an occasional cell was binucleated. A few giant cells with three or more nuclei clumped together in the

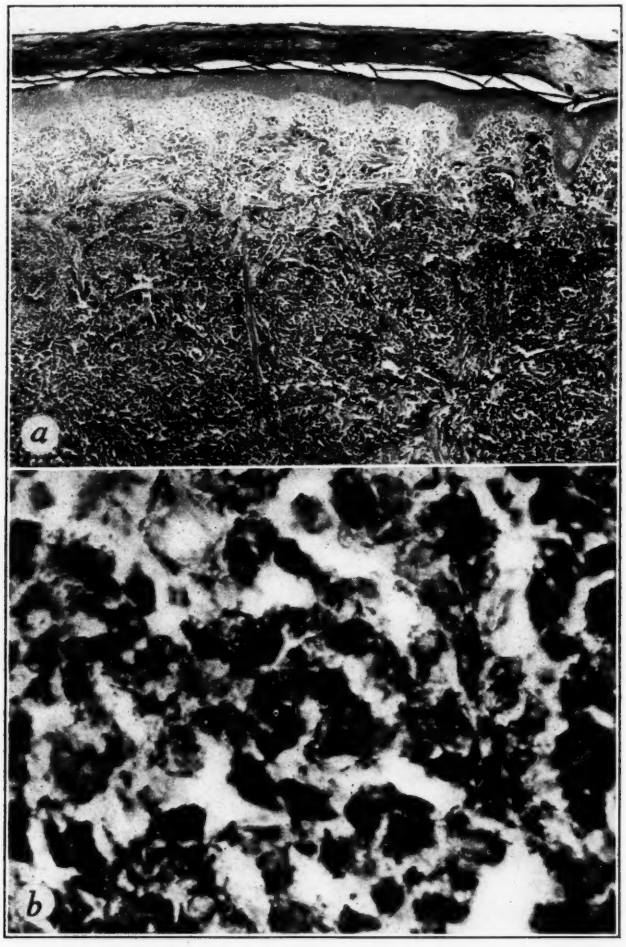

Fig. 2.—(*a*) Mast cells occupying the cutis and the subcutis (stained by the Giemsa method; × 42). (*b*) Large number of mast cells with their typical metachromatic granules (stained by the Giemsa method; × 750).

mass of granular cytoplasm were noted. Mitotic figures were absent. The papillae and the entire cutis were replaced with these groups and bundles of mast cells (fig. 2).

The patient was seen again by us after a lapse of two and a half years. The total number of lesions had remained the same, but the infiltration had disappeared in about a third of the lesions. No urtication on stroking the nodules or pigmented macules was obtained. The prothrombin time was within normal limits.

Unna,[4] in describing the childhood types of urticaria pigmentosa, stated that the lesions persist to about the time of puberty and then almost always spontaneously disappear. Finnerud [1] reported the loss of elevation of the nodules but gave no prognosis. It is the consensus of most authors that the nodules flatten out usually by puberty but that hyperpigmentation may remain indefinitely. Ormsby,[5] in discussing a case, stated that the lesions may persist from infancy until the patient is more than 30 years of age although they diminish in size after the eighteenth year.

Urticaria pigmentosa should be suspected in any patient if large pigmented nodules have been present since birth or shortly thereafter. Juvenile xanthomatosis, nevoxanthoendothelioma and myoblastoma must be differentiated. When the tissue removed for biopsy is stained with one of the basic aniline dyes, the mast cells with the metachromatic granules (color tone different from that of the dye employed) are easily recognized and the diagnosis established. It is sometimes necessary to employ the Giemsa stain rather than polychrome methylene blue in order to bring out the metachromatic granules.

Since these lesions of nodular urticaria pigmentosa are actually mast cell tumors, we wish to focus attention on the function of mast cells. The varied and conflicting opinions on the functions of the mast cells were ably discussed by Michels.[6] Holmgren and Wilander [7] in 1937 pointed out that the metachromatic material of the mast cells of the liver capsule is identical with heparin. Jorpes and co-workers [8] further verified this observation. In 1942 Bloom [9] first used the term "mastocytomas" in describing mast cell tumors, both malignant and benign, in the dog.

4. Unna, P. G.: The Histopathology of the Diseases of the Skin, New York, Macmillan & Co., 1896, p. 955.

5. Ormsby, O. S., in discussion on Oliver, E. A.: Urticaria Pigmentosa, Arch. Dermat. & Syph. **26**:520 (Sept.) 1932.

6. Michels, N. A.: The Mast Cells, in Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, pp. 235-372.

7. Holmgren, H., and Wilander, O.: Beitrag zur Kenntnis der Chemie und Funktion der Ehrlichschen Mastzellen, Ztschr. f. mikr.-anat. Forsch. **42**:242-278, 1937.

8. Jorpes, E.; Holmgren, H., and Wilander, O.: Ueber das Vorkommen von Heparin in den Gefässwänden und in den Augen: Ein Beitrag zur Physiologie der Ehrlichschen Mastzellen, Ztschr. f. mikr.-anat. Forsch. **42**:279-301, 1937.

9. Bloom, F.: Spontaneous Solitary and Multiple Mast Cell Tumors ("Mastocytoma") in Dogs, Arch. Path. **33**:661-676 (May) 1942.

Since that time Oliver, Bloom and Mangieri [10] have investigated the morphology and behavior of neoplastic mast cells cultivated in vitro and the cytochemical characteristics of mast cells; they have demonstrated massive heparin content of a tumor composed of well differentiated mast cells, and yet no anticoagulative activity was observed in vivo. There are no reports of hemorrhagic tendencies in cases of urticaria pigmentosa. Our patient presented no purpura or bleeding tendencies, and the blood coagulation time was well within normal limits.

Bali and Furth,[11] in citing Barnard,[12] tried to explain this parodoxic situation in which animals that bear tumors rich in mast cells fail to exhibit hemorrhagic tendencies. They proposed the theory that the blood mast cell of marrow origin is responsible for the production of heparin and that heparin regulates the thromboplastin content of the bone marrow.

In addition to liberating heparin the mast cell granules recently have also been shown to contain acid and alkaline phosphatases and cytochrome oxidase lipids.

Heparin or a heparin-like substance has also been found in the blood of dogs in anaphylactic shock in greater amounts than are normally present. It has not been shown to be present in man in any allergic manifestation, but with regard to this point one again can speculate on the association between the mast cells and local urtication in urticaria pigmentosa.

SUMMARY

A case of urticaria pigmentosa of the nodular type is reported as a diagnostic problem. The diagnosis was established microscopically only after the Giemsa method of staining was used. In this disease the prognosis is good, most of the lesions disappearing after puberty. In our case a third of the lesions had lost their infiltration and were macules at the time of writing. Inasmuch as urticaria pigmentosa is characterized by the presence of mast cell tumors, the close association of heparin and mast cell granules is discussed. The finding of large amounts of heparin in mast cell tumors in dogs is noted, as well as the lack of anticoagulant effects in vivo. Heparin has also been found in anaphylactic shock in dogs.

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10. Oliver, J.; Bloom, F., and Mangieri, C.: On the Origin of Heparin: An Examination of the Heparin Content and the Specific Cytoplasmic Particles of Neoplastic Mast Cells, J. Exper. Med. **86**:107-116 (Aug. 1) 1947.

11. Bali, T., and Furth, J.: A Transplantable Splenic Tumor Rich in Mast Cells: Observations on Mast Cells in Varied Neoplasms, Am. J. Path. **25**:605-619 (July) 1949.

12. Barnard, R. D.: Similarity to Heparin of the Clotting Inhibitor in Acute Leukemia and the Significance of Hyperheparinemia in Estrapenic Cholinergic States, Science **107**:571-572 (May 28) 1948.

FAILURE OF MODERN FOOTWEAR TO MEET BODY REQUIREMENTS FOR PSYCHIC AND THERMAL SWEATING

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A DISSECTION of over 500 shoes worn by patients with foot eruptions disclosed that the materials used in the fabrication of this footwear were moisture repellent. The uppers and soles, if not made of materials naturally resistant to moisture, were treated to increase their moisture-proof properties. Adhesives used on the inside sealed any moisture leaks in the outer construction. Heel linings were coated to prevent the penetration of sweat. Droplets of condensed sweat have been seen on such linings in cool weather. The moisture-proof incasement around the heel does allow escape of some sweat vapor, but the opposite holds true for the distal two thirds of the foot. Shoes are laced or strapped on the feet, the tongue, vamp and insole arch forming a snug collar. Moisture tends to seal this collar, impeding the exit of sweat vapor and the entrance of air, especially when the person is inactive. The distal portion of the foot is kept in a water-proof compartment by linings, toe boxes, insoles and bottom fillers. Adhesives seal the porosity of naturally absorbent materials. These compartments are shown in figure 1. Shoes that keep environmental water out also keep in psychic and thermal sweat. Even sandal straps with impervious linings cause hydration of the epithelium of the foot at the line of contact.

QUALITATIVE INCIDENCE OF PSYCHIC SWEATING

In the fall the physicians in Evansville carry out physical examinations of male high school students. Doing so has provided [1] an opportunity for us to observe the incidence of psychic sweating. The skin station was seventh in the examining line. Each student was under examinational stress. The palm (L. E. G.) was used to detect a dry or moist condition of the palms, armpits and soles. Visible sweating was denoted as wet. Only 2 subjects out of 1,267 were sweating on their face. The lack of uniformity in psychic sweating is apparent from table 1. Subjects with their feet dripping sweat would have palms and armpits fairly dry. No difference was noted between blonds and brunets. Moist to wet palms, armpits and soles are normal biologic responses.

1. Courtesy of Mr. E. W. Weber.

Silverman and Powell [2] noted an intense sweating response on the palms and soles in 25 per cent of 1,100 Army patients and a demonstrable type of sweating in 80 per cent. Sweating is continuous on the palms, armpits and soles. Fear, anger, joy, anxiety and mental work greatly increase it, often to the point of profuseness. Moist fingers are necessary for grasping objects. A moist sole allows the skin to become fixed at the moment of traction. The degree of moisture, grasping force and kind of object all influence the holding power of the hand. The ridges on the palms and fingers and soles and toes, plus moisture, produce a vacuum cup–like action. An analogy may be seen in comparison of the degree of adhesion between two pieces of dry paper with that between a dry one and a moist one. Moist palms and soles apparently have a biologic "readying" action. The center for the grasp reflex and that for psychic sweating are closely associated in the brain cortex.[3]

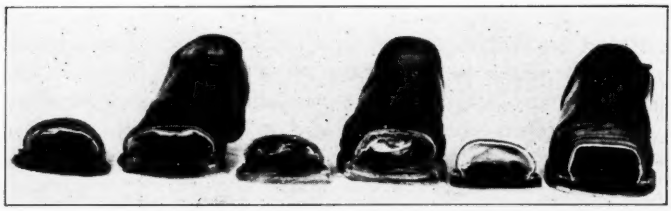

Fig. 1.—These three shoes represent the footwear wardrobe of patient C. O. The shoe to the left had an inner canvas sock lining, cemented to an asphalt toe box. The linings were worn through, with the dorsum of the toes impinging on the asphalt. The toe box was cemented to another canvas lining, which in turn was cemented to the leather upper. The cements were powdery. A thin leather insole was cracked and discolored, with portions of it missing. The bottom filler was an asphalt cork material. Beneath these materials were two layers of red rubber, cemented to the filler. The sole was leather, cemented to the rubber.

The middle shoes had a laminated cloth toe box cemented to a steel toe box. The box was worn through by the big toe. Red sponge rubber cemented the leather of the uppers to the steel toe box. The leather insole was cracked and fissured. The bottom filler was a plastic material. The sole was leather.

The shoe to the right had a cloth, laminated toe box, worn through by the big toe. A leather insole rested on a plastic sawdust filler. Beneath this was an inner sole of black rubber, cemented to an outer sole of red rubber.

Lacing the feet into these shoes places them in an environment from which moisture cannot escape. The toes are surrounded by moisture-repellent materials. The wet foot is subjected to the irritants and sensitizers present in materials used in the fabrication of the shoes.

The intimate relation between psychic activity and sweating suggests that sweating is sort of a "safety valve" for releasing emotional tension, increasing mental stress causing greater sweating. The substance pro-

2. Silverman, J. J., and Powell, V. E.: Studies on Palmar Sweating, Am. J. M. Sc. **208**:297, 1944.

3. Literature cited by Silverman and Powell.[2]

ducing the tension or "nerves" may be excreted in sweat or tears. If the tension becomes critical and sweating can no longer keep the balance, crying begins to restore the balance. The incidence of sweating associated with crying was determined in 84 subjects (table 2). Fifty-three per

TABLE 1.—*Qualitative Incidence of Psychic Sweating*

Area of Psychic Sweating							
			Date	9-15-49	9-22-49	10-6-49	10-13-49
			Air Temperature, F.	59	77	72	68
			Air Humidity, %	91	89	73	39
Palms	Armpits *	Soles		School 1	School 2	School 3	School 4
Moist	Moist	Moist		173	96	154	108
Moist	Wet	Moist		98	70	49	54
Wet	Wet	Wet		16	53	37	15
Moist	Wet	Wet		12	10	38	32
Wet	Wet	Moist		11	..	12	8
Moist	Dry	Moist		23	..	..	..
Wet	Dry	Moist		4	..	1	12
Dry	Wet	Moist		2	..	7	..
Wet	Dry	Wet		3	..	1	11
Moist	Dry	Wet		4	..	..	..
Dry	Dry	Moist		4	..	..	2
Moist	Wet	Dry		4	4	4	11
Wet	Wet	Dry		1	3	..	..
Dry	Dry	Dry		9	3	2	5
Dry	Dry	Wet		3	..	1	..
Wet	Moist	Wet		9	13	24	19
Wet	Moist	Moist		..	21	..	..
Moist	Moist	Dry		..	9	2	..
			Total	376	282	332	277
Number of blond subjects				283	183	155	160
Number of brunet subjects				93	99	177	117
Number of moist soles				315	187	223	184
Number of wet soles				47	76	101	77
Grand percentage of moist and wet soles, 95.5%							

* Thermal sweating also.

TABLE 2.—*Incidence of Psychic Sweating During Crying*

Psychic Sweating	No. of Subjects
Yes	45
No	18
?	21
Incidence, 53.6 per cent	

Emotional State Producing Crying	No. of Subjects
Quarrel	13
Death	13
Self-pity	15
Fear	4
Joy	6
Anger	3
Motion picture	14
Family trouble	8
Sickness	5
Unknown	3

Emotional State After Crying	No. of Subjects
Relieved	66
Depressed	18

cent were aware of psychic sweating during the crying period, and 78 per cent were relieved of emotional tension by crying.

Kuno [4] studied the difference between psychic and thermal sweating. Environmental temperature and humidity do not influence psychic sweating until such elevations occur as to produce generalized thermal sweating. Now the psychic areas except the armpits practically

4. Kuno, Y.: The Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934.

cease sweating. Burch and others[5] determined the rate of water loss from the skin of the foot in normal persons and in subjects with trench foot. In a comfortable environment the sole lost more sweat than the dorsal skin, but when the environment was made uncomfortably hot and humid greater sweating occurred from the dorsal aspect of the foot than from the sole. It is amazing that the seasonal incidence of tinea pedis coincides with thermal sweating of the feet whereas the chronic and recurrent cases are observed in the psychic sweaters.[6] Shoes made of moisture-repellent materials deny the existence of psychic and thermal sweating of the feet. Such footwear actually becomes a trap for this sweat.

QUANTITY OF SWEAT IN FOOTGEAR

Shoes and socks were dried on a rack over a steam boiler. The temperature varied between 33 C. (91.4 F.) and 35 C. (95 F.). Drying was carried out for two to three days. The shoes were then worn during the day in dry weather. Each subject was cautioned about stepping into any water or mud. The shoes and socks were weighed on removal. Drying was carried out for two to three days and the shoes weighed. The quantity of sweat is shown in table 3.

All subjects in groups A, B, C and D wore shoes made of materials that allowed condensation of sweat vapors. A 4 year old child retained as much as did a 45 year old adult, and female, as much as did male subjects. The temperature and humidity did not vary enough to affect the retention greatly. At lower or higher temperatures and humidities the results may have been different. The activities of the subjects appeared to be inconsequential. The quantity of sweat in the right and in the left shoe tended to be equal. Differences noted may have been due to the subject's standing on one foot or sitting with the legs crossed. Water-proofed footwear makes the feet perform their work with the pedal skin in a continually moist to wet environment.

THE EFFECT OF DIFFERENT MATERIALS ON THE QUANTITY OF SWEAT

These data were obtained on subjects in the hospital. Nylon was placed next to the skin, as it is when stockings are worn. This is a synthetic fiber, nonabsorbent but porous. The feet were wrapped in cotton, secured in place by several layers of gauze. Cotton is a plant fiber, absorbent and porous. A plastic sheeting was then wrapped around the feet and held in place with safety pins. This plastic

5. Burch, G. E.; Myers, H. L.; Porter, R. R., and Schaffer, N.: Rate of Water Loss from the Skin of the Foot of Normal and Trench Foot Subjects, Am. J. Physiol. **146**:37, 1946.

6. Gaul, L. E., and Underwood, G. B.: Primary Irritants and Sensitizers Used in the Fabrication of Footwear, Arch. Dermat. & Syph. **60**:649 (Nov., pt. 1) 1949.

TABLE 3.—*Amount of Sweat in Footgear Under Wearing Conditions in Dry Weather*

Subject and Date	Age and Sex	Maximum Air Temperature, F.	Maximum Air Humidity, %	Activity	Hours Worn	Type of Shoe	Amount of Sweat, Right Shoe, Gm.	Amount of Sweat, Left Shoe, Gm.	Amount of Sweat, Both Shoes, Gm.
1949									
Group A									
T. W. 9-17	19 M	83	95	Loafing	7	Brown oxford, rubber sole	16	18	..
W. Z. 9-19	27 M	79	88	Selling	6	Brown oxford, leather sole	21	27	..
W. Z. 9-22	27 M	77	89	Selling	6	Brown oxford, rubber sole	46	44	..
L. G. 9-20	45 M	76	92	Office work	14	Brown oxford, leather sole	16	18	..
L. G. 9-21	45 M	83	95	Office work	8	Black oxford, leather sole	18	10	..
R. C. 9-20	31 F	76	92	Housework	7	White oxford, rubber sole	5	5	..
J. R. 9-20	19 M	76	92	Selling	7	Brown oxford, rubber sole	16	16	..
J. R. 9-21	19 M	83	95	Selling	7	Brown oxford, leather sole	18	18	..
G. M. 9-20	22 M	76	92	Driving	10	Brown loafer, leather sole	19	18	..
E. L. 9-20	25 F	76	92	Bed rest	9	White platform sandal	7	9	..
J. G. 10-15	4 F	72	38	Playing	8	White oxford, rubber sole	14	16	..
Group B									
J. M. 10-14	23 M	72	43	Office work	9	Brown oxford, rubber sole	16	21	..
T. T. 10-14	30 M	72	43	Office work	9	Brown oxford, leather sole	30	28	..
R. H. 10-14	19 M	72	43	Office work	9	Brown oxford, rubber sole	36	32	..
P. B. 10-14	23 M	72	43	Office work	9	Brown oxford, leather sole	19	25	..
C. R. 10-14	18 M	72	43	Office work	9	Brown oxford, rubber sole	27	27	..
Group C									
M. S. 10-15	23 F	72	38	Office work	8	White oxford, rubber sole	14	12	..
W. M. 10-15	24 F	72	38	Office work	8	White oxford, rubber sole	23	30	..
M. F. 10-15	34 F	72	38	Office work	8	White oxford, rubber sole	10	12	..
Group D									
R. D. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	56
B. W. 10-14	15 M	72	43	Basketball practice	2	Tennis shoes	..	..	33
B. P. 10-14	15 M	72	43	Basketball practice	2	Tennis shoes	..	..	43
D. T. 10-14	15 M	72	43	Basketball practice	2	Tennis shoes	..	..	40
B. M. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	38
J. W. 10-14	18 M	72	43	Basketball practice	2	Tennis shoes	..	..	56
B. W. 10-14	15 M	72	43	Basketball practice	2	Tennis shoes	..	..	59
J. F. 10-14	18 M	72	43	Basketball practice	2	Tennis shoes	..	..	65
B. S. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	46
J. W. 10-14	17 M	72	43	Basketball practice	2	Tennis shoes	..	..	55
J. H. 10-14	18 M	72	43	Basketball practice	2	Tennis shoes	..	..	40
B. S. 10-14	17 M	72	43	Basketball practice	2	Tennis shoes	..	..	38
M. H. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	42
J. C. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	65
B. H. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	68
D. T. 10-14	18 M	72	43	Basketball practice	2	Tennis shoes	..	..	44
V. P. 10-14	16 M	72	43	Basketball practice	2	Tennis shoes	..	..	53
J. B. 10-14	15 M	72	43	Basketball practice	2	Tennis shoes	..	..	35
J. K. 10-14	17 M	72	43	Basketball practice	2	Tennis shoes	..	..	66

material was water proof. On their removal the dressings were weighed. Drying was carried out as with the footgear. The drying temperatures approximated the foot temperatures. The findings are shown in table 4.

The results demonstrate the degree of wetting of the pedal skin by impervious materials. Every plastic wrapping removed showed condensed moisture on the inside. The plastic material increased the quantity of moisture around the foot two, four and even thirty times. Nylon did not influence the degree of sweating. The quantity of sweat observed when only cotton and gauze wrappings were put on the feet demonstrated the rapid evaporation of sweat from these absorbent and porous materials. A dry eczematization of the hands in subject E. L. was associated with a greater output of pedal sweating. After the hands began to sweat, the output from the feet decreased. Similar clinical observations have been made on 5 patients. A dry eczematization of the feet caused a more profuse sweating on the hands. This observation raises an important question: Does blockage of psychic sweating at one area produce a greater outflow at the other areas? Perhaps even the use of antiperspirants in the armpits may affect the balances. When shoes are constructed to prevent evaporation of sweat, with the increased heat production from exercise and with no way for this heat to be dissipated by evaporation, it is only natural that there should be an increased amount of sweating on the hands.[7] For 3 subjects the temperatures were taken inside the plastic-covered dressings. They varied from 32 C. (89.6 F.) to 38 C. (100.4 F.). Further study of this problem may shed more light on the causes of hyperhidrosis. Subjects E. L. (Sept. 30, 1949) and H. F. were aware of filling their dressings with sweat during a visit with relatives.

TABLE 4.—*Influence of Various Materials on the Quantity of Sweat*

	Maximum Weight of Dressing	Maximum Weight of Dressing on Removal	Amount of
			After

INCREASED SUSCEPTIBILITY OF WET SKIN TO PENETRATION BY IRRITANTS AND SENSITIZERS

The placing of an impervious material next to the skin is soon followed by an accumulation of moisture beneath the covering. Hot weather increases the amount. The occluded skin becomes sticky and hydrated, and symptoms produced are usually referred to as uncomfortable or annoying. The following reports of cases illustrates the increased susceptibility of a wet or moist skin to contactants.

CASE 1.—C. R., a 2 year old white girl, presented a papular and papulovesicular dermatitis, the distribution of which corresponded to the points of contact with the sheet of one accustomed to sleeping on the left side. The last of April 1949 the mother had purchased a rubber crib sheet. On May 13, the eruption appeared, its development having been aided by the child's having wet the bed. A patch test with a piece of the rubber was applied on the right shoulder, and on the left arm

7. Roth, G. M.: Personal communication to the authors.

TABLE 4.—*Influence of Various Materials on the Quantity of Sweat*

Subject and Date	Age	Sex	Maximum Air Temperature	Maximum Air Humidity	Location	Dressings	Hours Worn	Weight of Dressing on Removal, Gm.	Weight of Dressing After Drying, Gm.	Amount of Sweat, Gm.
1949										
E. L.	25	F	78	96	Right foot	..... Cotton Gauze Plastic	19	210	196	14
					Left foot	..... Cotton Gauze Plastic	19	236	221	15
9-26 (Hands eczematized, not sweating)										
9-29 (Night)	..	..	62	86	Right foot	..... Cotton Gauze	20	63	61	2
					Left foot	..... Cotton Gauze	20	65	63	2
9-30	..	..	68	96	Right foot	Nylon Cotton Gauze Plastic	8	172	150	22
					Left foot	..... Cotton Gauze Plastic	8	165	143	22
10-3 (Hands sweating)	..	..	67	94	Right foot	..... Cotton Gauze Plastic	8	152	141	11
					Left foot	..... Cotton Gauze Plastic	8	117	108	9
					Right hand	..... Cotton Gauze Plastic	8	100	91	9
					Left hand	..... Cotton Gauze Plastic	8	140	131	9
W. B.	45	M	67	94	Right foot	..... Cotton Gauze Plastic	5	162	148	14
10-3					Left foot	..... Cotton Gauze Plastic	5	209	195	14
					Right hand	..... Cotton Gauze Plastic	5	159	145	14
					Left hand	..... Cotton Gauze Plastic	5	153	140	13
10-5	..	..	68	95	Right foot	..... Cotton Gauze Plastic	8	190	170	20
					Left foot	..... Cotton Gauze	8	178	173	5
					Right hand	..... Cotton Gauze	8	86	81	5
					Left hand	..... Cotton Gauze Plastic	8	140	119	21
10-6 (Night)	..	..	72	73	Right foot	..... Cotton Gauze Plastic	9	154	137	17
					Left foot	..... Cotton Gauze	9	67	63	4
H. F.	24	M	84	56	Right foot	..... Cotton Gauze	11	109	107	2
10-10 (Night)					Left foot	..... Cotton Gauze Plastic	11	263	198	65
					Right hand	..... Cotton Gauze	11	95	93	2
					Left hand	..... Cotton Gauze Plastic	11	214	154	60
L. F.	53	F	72	54	Right foot	..... Cotton Gauze Oiled silk	11	107	100	7
10-16 (Night)					Left foot	..... Cotton Gauze	11	53	51	2
10-18	..	..	77	49	Right foot	Nylon Cotton Gauze	5	55	55	0
					Left foot	..... Cotton Gauze	5	50	50	0
10-20	..	..	81	61	Right foot	Nylon Cotton Gauze Oiled silk	4	74	70	4
					Left foot	..... Cotton Gauze Oiled silk	4	69	65	4
R. H.	50	M	72	54	Right foot	..... Cotton Gauze Plastic	16	224	199	25
10-16 (Night)					Left foot	..... Cotton Gauze	16	140	128	12
					Right hand	..... Cotton Gauze	16	102	89	13
					Left hand	..... Cotton Gauze Plastic	16	205	179	26
10-17	..	..	77	54	Right foot	..... Cotton Gauze Plastic	6	184	169	15
					Left foot	..... Cotton Gauze Plastic	6	163	148	15
10-20	..	..	81	61	Right foot	Nylon Cotton Gauze Plastic	7	199	189	10
					Left foot	..... Cotton Gauze Plastic	7	184	175	9
					Right hand	..... Cotton Gauze Plastic	7	161	147	14
					Left hand	Nylon Cotton Gauze Plastic	7	149	137	12
E. L.	49	M	77	54	Right foot	..... Cotton Gauze	7	103	103	0
10-17 (Night)					Left foot	Nylon Cotton Gauze	7	103	102	1
J. D.	8	M	77	54	Right foot	Nylon Cotton Gauze	10	33	33	0
10-17 (Night)					Left foot	..... Cotton Gauze	10	29	29	0
P. O.	4	F	77	54	Right foot	..... Cotton Gauze	10	37	35	2
10-17 (Night)					Left foot	Nylon Cotton Gauze	10	38	38	0
C. O.	38	F	77	54	Right foot	Nylon Cotton Gauze Plastic	7	167	163	4
10-17 (Night)					Left foot	..... Cotton Gauze Plastic	7	135	133	2
D. W.	74	M	77	54	Right foot	..... Cotton Gauze	7	57	57	0
10-17					Left foot	Nylon Cotton Gauze	7	89	87	2
A. H.	35	F	77	54	Right foot	Nylon Cotton Gauze Plastic	8	109	105	4
10-17					Left foot	..... Cotton Gauze Plastic	8	161	154	7

a strip of the rubber was secured with slight tension. Twenty-four hours later, the reaction to the patch test was doubtful but at the site of the rubber strip a sharply outlined band of erythema and edema stood out.

Case 2.—C. F., a white nurse aged 25, was seen for a recurrent dermatitis of the ears, neck, eyelids, hands, genitals and feet. The attacks were traced to elastic in hair nets, rubber gloves, elastic in pants and rubber adhesive in shoes. Patch tests produced only a slight erythema which disappeared in forty-eight hours. The elastic taken from the pants was secured with slight tension just above the right elbow. Within twenty-four hours a flare type reaction appeared, consisting of a papular, highly pruritic dermatitis. During the next forty-eighty hours the left arm reacted with a similar eruption and symptoms. A unilateral dermatitis due to rubber commonly becomes bilateral. Inspection of the sensitization dermatitis on the left arm ten days later disclosed linear lichenification, and many of the lesions had been scratched open. Rubber allergens appear to rapidly keratinize sweat and sebaceous gland orifices.

Case 3.—M. G., a 4 year old white girl, presented a linear dermatitis on the back, dorsal surfaces of the arms and flexor surfaces of the thighs. She had been playing in the water with an inflated tire tube. The distribution of the dermatitis corresponded to the points of contact encountered while she was resting on the tube. A patch test with the tube produced a doubtful reaction. A strip of the tube secured around the arm produced the initial dermatitis.

Case 4.—N. S., a 7 month old white girl, was observed for a generalized dermatitis. The duration was two weeks, and the onset coincided with the purchase of a plastic crib sheet. Often the mother noted the child sleeping in direct contact with the sheet. A strip of the sheet placed around the arm reproduced in twenty-four hours the initial eruption. A patch test with the plastic produced a negative result.

Case 5.—C. W., a 60 year old white woman, presented an eruption which followed the hair line of the scalp. Questioning disclosed that the eruption had appeared after she had been wearing a new hair net. The elastic from the net was removed and secured around the arm. A patch test was also done on the shoulder. Forty-eight hours later the elastic band had reproduced the dermatitis. The reaction was much more intense in the axillary portion of the arm where sweat was present than on the lateral surface. The reaction to the patch test too was positive but much less intense.

Case 6.—E. C., a white housewife aged 49, had been wearing intermittently for six months a pair of green strap pumps. While fishing, she got her feet wet. Almost at once she was aware of a burning sensation of her feet. One hour later a dermatitis appeared, demarcated by the strap of the shoes.

These cases demonstrate the remarkable increased susceptibility of the skin to moisture-repellent materials. They even suggest the inadvisability of the exposure of the skin to such materials because they are bound to interfere with cutaneous functions, especially in hot weather. The current trend toward the use of moisture-proof materials for wearing apparel, seat covers and so on may prove a boomerang to the users. At a nearby club many of the members acquired during hot weather a dermatitis of the buttocks or back from sitting on chairs with plastic

upholstery. Shelley[*] and Melton[8] studied the factors accelerating the penetration of histamine. They found that when evaporation was prevented by the covering of the skin with an excess of histamine solution in a closed chamber, the absorption continued indefinitely. As the liquid vehicle evaporated, absorption abruptly terminated. Water, itself, proved an excellent vehicle for the absorption of histamine.

THE IMPORTANCE OF THE FEET IN THE REGULATION OF BODY TEMPERATURE

Air temperatures between 75 and 85 F. (24 to 30 C.) represent the zone in which there is normal physiologic regulation of body temperature. At lower temperatures the body adjusts itself by vasomotor constriction of peripheral blood vessels. Seventy per cent of the heat lost at temperatures below 85 F. is by radiation, convection and conduction. The degree of heat loss from the body varies with the air temperature, air movement, humidity, nature of clothing and quantity of heat produced. Air is a poor conductor of heat, and so loss by this means is minor except when the body is in contact with a cool object. At air temperatures above 85 F., body temperature is regulated by evaporation of sweat.[9] Sweating occurs subsequent to maximal vasodilatation of the peripheral vascular system.

Wearing water-repellent footgear which allows the feet to become wet with psychic or thermal sweat tends to keep the feet at environmental temperature. This point can be illustrated as follows: A subject has his hand in a pail of water at room temperature. Water is a much better conductor of heat than is air. Water conducts heat away from the hand. If the subject moved to a cooler environment, the water would gradually cool and the heat lost from the hand would increase. Profound vascular changes would accompany this continual dissipation of heat. Trench foot has been noted when the environmental temperature is at 32 F. (0.0 C.) or somewhat higher. If the feet are wet, moisture increases the loss of heat from the extremities.[10] Two subjects sitting at a football game with an air temperature of 32 F. would lose heat from their feet in proportion to the quantity of psychic sweat in their shoes. The greater the quantity of sweat, the greater the heat loss by conduction. If the subject with his hand in a pail of water moved to environments of increasing temperatures the loss of heat would decrease, and at sufficiently high temperatures heat would pass from the water

8. Shelley, W. B., and Melton, F. M.: Factors Accelerating the Penetration of Histamine Through Normal Intact Skins, J. Invest. Dermat. **13**:61, 1949.

9. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 4, Baltimore, Williams & Wilkins Company, 1945.

10. Allen, E. V.; Barker, N. W., and Hines, E. A.: Peripheral Vascular Diseases, Philadelphia, W. B. Saunders Company, 1946, p. 256.

into the hand. Wearing water-proof footwear at an environmental temperature of 85 F. brings in another source of moisture, or thermal sweating. The humidity directly influences the quantity of sweat. Heat loss by convection—movement of air around the feet—is considerable at the heel but minimal for the distal two thirds of the foot. Sitting or standing reduces heat loss by convection to a minimum. A person working in an office at 75 F. with a humidity of 50 per cent would have a certain amount of psychic sweat in his shoes. His going outdoors to a temperature at 32 F. and a humidity of 30 per cent would suddenly increase evaporation, with resulting excessive cooling of the feet.

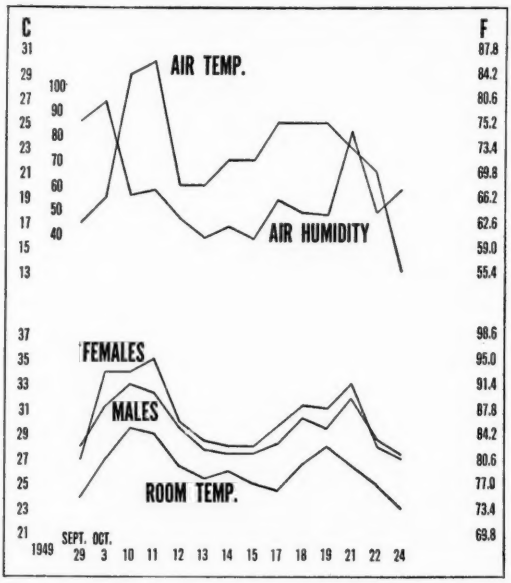

Fig. 2.—The correlation between shoe temperature and room temperature and the relation of humidity to shoe temperature are charted. Female subjects were aged 24, 24 and 32 and wore white nurses' oxfords with rubber soles and nylon hose. Two were active, and 1, moderately active. The male subjects were aged 45 and 65. One wore woven leather shoes and cotton hose, and the other, leather shoes and cotton hose. One was active, and the other, moderately active.

Various portions of the body play different roles in the elimination of heat. Increasing environmental temperature or increasing production of heat causes a shift of blood to the extremities for cooling. Sheard, Roth and Horton [11] demonstrated that under environmental conditions of 77 F. (25 C.) and 40 per cent humidity the temperature of the toes

11. Sheard, C.; Roth, G. M., and Horton, B. T.: Relative Role of Extremities in Heat Dissipation, Arch. Phys. Therapy **20**:133, 1949.

was slightly above room temperature. As the room temperature is increased, heat is dissipated, first by the hands and forearms and then by the regulatory control of the feet and legs. At higher temperatures, 85 to 90 F. (30 to 32 C.), the temperature of the hands and feet is the same as that of the forehead. Footwear that prevents evaporation of psychic and thermal sweats not only cripples heat loss from the feet but disturbs the temperature-regulating capacity of the entire body. Heat loss from the feet is primarily by conduction, which is influenced remarkably by environmental temperature and humidity. Heat loss by convection is relatively minor. Posture affects the skin temperature of the feet,[11] and ingestion of food is followed by increased heat production. We have all observed facial sweating in people during a course of a meal. Perhaps this annoyance might be minimized if the shoes they were wearing allowed evaporation of sweat. Interestingly,

TABLE 5.—*Shoe Temperatures Under Wearing Conditions*

Date	Air Temperature, F.	Air Humidity, %	Room Temperature	No. of Subjects	Lowest Shoe Temperature, C.	Highest Shoe Temperature, C.	Average Shoe Temperature, C.
9-29-49	62	86	24.0 C. (75.2 F.)	12	23.5	32.0	28.0
9-30-49	68	96	25.0 C. (77.0 F.)	10	23.0	32.0	28.0
10-1-49	76	95	27.0 C. (80.6 F.)	10	29.0	34.0	31.9
10-3-49	67	94	27.0 C. (80.6 F.)	9	27.5	34.0	30.9
10-5-49	68	96	27.0 C. (80.6 F.)	7	28.0	33.0	30.3
10-11-49	85	58	29.5 C. (85.1 F.)	7	32.0	35.0	33.4
10-12-49	68	47	27.0 C. (80.6 F.)	7	29.0	32.5	30.2
10-13-49	68	39	25.0 C. (77.0 F.)	5	28.5	30.0	28.8
10-14-49	72	43	24.5 C. (76.1 F.)	8	28.0	32.0	30.2
10-15-49	72	38	24.5 C. (76.1 F.)	6	29.5	32.0	30.0
				Total, 81			

people unconsciously avoid this discomfort by slipping their shoes off whenever possible, and women do so even in public places such as restaurants and motion picture theaters.

Shoes that prevent the evaporation of psychic and thermal sweat from the feet profoundly affect the body temperature. Warming or cooling of the feet produces a reflex warming or cooling of the hands.[12]

THE RELATION OF ENVIRONMENTAL TEMPERATURE AND HUMIDITY TO SHOE TEMPERATURE

Shoe temperatures under wearing conditions were determined by the slipping of a thermometer along the medial aspect of the foot. The bulb rested near the medial ball of the foot. The data concerning 5

12. Fatherree, T. J., and Allen, E. V.: Sympathetic Vasodilator Fibers in the Upper and Lower Extremities: Observations Concerning the Mechanism of Indirect Vasodilatation Induced by Heat, Arch. Int. Med. **62**:1015 (Dec.) 1938. Gibbon, J. H., Jr., and Landis, E. M.: Vasodilatation in the Lower Extremities in Response to Immersing the Forearms in Warm Water, J. Clin. Investigation **11**:1019 (Sept.) 1932.

subjects are shown in figure 2. Shoe temperature tended to fluctuate with the room temperature. The effect of humidity on shoe temperature was demonstrated on October 17 and again on October 21. Table 5 shows the observations made on 79 subjects.

DIFFUSION OF WATER VAPOR THROUGH SHOE MATERIALS

Experiments were performed to determine the ease with which shoe materials allowed the passage of water vapor. Pint (473 ml.) self-sealing fruit jars were filled about half full of water. Shoe materials were substituted for the sealing disks. The specimens were weighed and kept at the temperatures shown in figure 3. The differences in diffusion

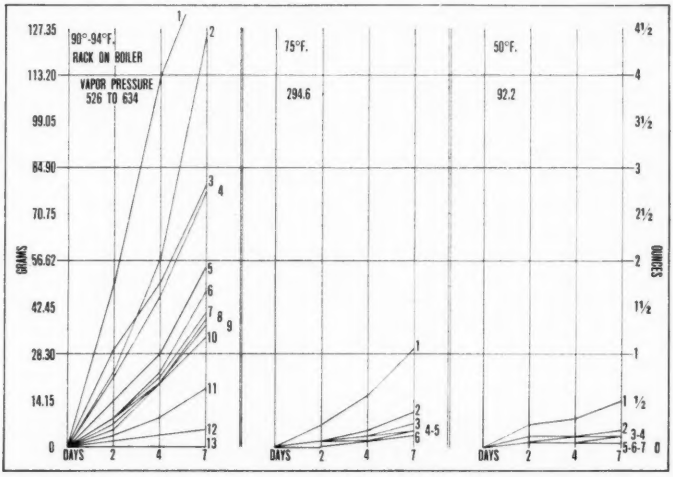

Fig. 3.—Charts showing the effect of temperature on diffusion rates of water vapor through shoe materials. All materials were 5.7 cm. in diameter. Vapor pressure of the water was measured in millimeters of mercury. In the first section of the chart, the shoe materials and their thicknesses were as follows: *1,* control; *2,* canvas, 1 mm.; *3,* leather (extracted in ether, twenty-four hours), 3 mm.; *4,* leather (extracted in water, twenty-four hours), 3 mm.; *5,* leather, 3 mm.; *6,* cemented leather, 2 mm.; *7,* cemented canvas, 1 mm.; *8,* one layer of leather, 3 mm.; *9,* tan-coated leather, 1 mm.; *10,* two layers of leather, 6 mm.; *11,* three layers of leather, 9 mm.; *12,* composition, 3 mm., and *13,* composition, 3 mm. In the second section of the chart, explanations are as follows: *1,* control; *2,* canvas, 1 mm.; *3,* cemented canvas, 1 mm.; *4,* tan-coated leather, 1 mm.; *5,* cemented leather, 2 mm., and *6,* leather, 3 mm. The shoe materials and their thicknesses indicated in the third section of the chart were these: *1,* control; *2,* canvas, 1 mm.; *3,* cemented canvas, 1 mm.; *4,* cemented leather, 2 mm.; *5,* leather, 3 mm.; *6,* tan-coated leather, 1 mm., and *7,* composition, 3 mm.

rates of materials were plotted. The effects of adhesives and coatings are apparent. An interesting coincidence was the discovery that the boiler temperature roughly paralleled the shoe temperature. Thus, the

vapor pressure of the boiler specimens approximated the vapor pressure in shoes. Two leather specimens were placed in basins of water and covered with bell jars. At this high humidity around the specimens, one of the specimens actually gained water; so the diffusion rate then is also governed by the relative humidity. Shoe materials that lessen or prevent the passage of water vapors interfere with sweat evaporation from the feet.

CONCLUSIONS

The foot portion of socks and hose should be made of absorbent fibers, readily permitting the transference away from the feet of psychic and thermal sweat. Shoe materials should allow the rapid passage of water vapor so that evaporation from the feet can play its important role in the regulation of foot and body temperature. The skill of athletes should be enhanced by the wearing of footgear that meets physiologic requirements. Environmental water can be kept away from the feet by such means as loose-fitting overshoes or galoshes.

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DIIODOHYDROXYQUINOLINE IN DERMATOLOGIC THERAPY

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AS A RESULT of preliminary trials with diiodohydroxyquinoline (diodoquin®) as a topical therapeutic agent,[1] we reported that (1) satisfactory antibacterial and antifungal effects were obtained, (2) irritation and sensitization failed to occur even in dermatoses that are frequently intolerant and (3) the staining effect of the drug was comparatively trivial.

Diiodohydroxyquinoline (5,7-diiodo-8-hydroxyquinoline) is a fine pale yellow powder containing 63.9 per cent of iodine which is used orally in the treatment of amebiasis and other protozoal intestinal infections and vaginally (in the preparation floraquin®) in the treatment of trichomonas infection. Diiodohydroxyquinoline is insoluble in water, dilute acids and alkalis and is readily incorporated into ointments. Chemically it is closely related to certain other commonly used quinoline derivatives[2]: quinolor,® a mixture of 5-chlor-8-hydroxy-

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1. Leifer, W., and Steiner, K.: Diodoquin as a Topical Therapeutic Agent in Cutaneous Disease, J. Invest. Dermat. **12**:203 (April) 1949.

2. (*a*) Sulzberger, M. B., and Baer, R. L.: Vioform in Dermatologic Therapy, Arch. Dermat. & Syph. **58**:224 (Aug.) 1948. (*b*) Wise, F., and Sulzberger, M. B.: The Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1943. (*c*) Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy in General Practice, ed. 2, Chicago, The Year Book Publishers, Inc., 1942. (*d*) Sulzberger, M. B.: The 1946 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1947. (*e*) Peck, S. M., and Chargin, L.: Sycosis Vulgaris: A New Method of Treatment, Arch. Dermat. & Syph. **29**:456 (March) 1934. (*f*) Haeffner, A., and Kym, O.: Therapy of Mycosis of Feet: Sterosan Paste, Schweiz. med. Wchnschr. **77**:1369 (Dec. 27) 1947. (*g*) Sigg, K.: Sterosan in Mycosis of Feet and Mycotic Eczema, ibid. **77**:123 (Jan. 18) 1947. (*h*) Bloechlinger, L.: Dusting Powder Containing N-Dimethyl-Acroyl-Sulfanilamide and Sterosan, Praxis **35**:291 (May 9) 1946. (*i*) Brunn, G.: Sterosan Therapy,

quinoline, 7-chlor-8-hydroxyquinoline and 5,7-dichlor-8-hydroxyquinoline; iodochlorohydroxyquinoline (vioform®), 5-chloro-7-iodo-8-hydroxyquinoline; "sterosan," 5,7-dichlor-8-hydroxyquinaldine, and "surfen," a German proprietary quinoline derivative.

We are in accord with Tate [3] concerning the quinoline derivatives that "their employment in dermatology merits much further study." The present report deals with 150 patients and represents a considerable expansion of our preliminary trials.

PROCEDURE

The 150 patients included 70 hospitalized and 80 ambulatory persons. Hospitalized patients were examined daily, and almost all returned for periodic follow-up examinations after their discharge. Routine laboratory examinations were performed on all. Cultures for pyogenic micro-organisms were made prior to treatment, and direct examinations and cultures for fungi were carried out when the clinical diagnosis was questionable.

Ambulatory patients were instructed as to the exact use of the diiodohydroxyquinoline preparations, and they were observed at least once weekly. Laboratory studies were made on these patients only when indicated.

Diiodohydroxyquinoline was prescribed routinely in a concentration of 3 per cent. However, in highly irritable cases of acute dermatitis, treatment was initiated with concentrations of only 1 per cent. The concentration was gradually increased to 10 per cent in chronic or resistant cases, and in a few instances to 15 per cent.

Three to 5 per cent coal tar solution was often used with the higher concentrations of diiodohydroxyquinoline. In these cases it was felt that diiodohydroxyquinoline had produced its maximal benefit and that a "stimulating" medication was required to complete healing. For similar reasons, other medications were used with or following application of diiodohydroxyquinoline, such as zincundecate (desenex®) ointment, 5 per cent salicylic acid or half strength benzoic and salicylic acid (Whitfield's) ointment.

Aquaphor® (an oxycholesterol-petrolatum ointment base) served as the standard ointment vehicle. Hydrophilic ointment U. S. P. XIII, hydrous wool fat, petrolatum, zinc oxide paste and a simple shake lotion were also utilized as vehicles in certain situations. In our experience diiodohydroxyquinoline proved to be incompatible only with zinc emulsion. As a rule the ointment was rubbed in well but lightly two or three times a day and was not covered by a dressing.

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ibid. **34**:608 (Oct. 25) 1945. (*j*) Hotz, A., and Frutiger, U.: Sterosan, Schweiz. med. Wchnschr. **74**:680 (June 20) 1944. (*k*) Bertlich, H.: Vioform Therapy of Epidermophytosis of Miners, Deutsche med. Wchnschr. **65**:757 (May 12) 1939. (*l*) von Schuerer, F., and Homma, H.: Surfen: New Superficial and Deep Antiseptic, München. med. Wchnschr. **84**:1524 (Sept. 24) 1937. (*m*) Requé, P. G.: Vioform Ointment in Dermatology, Mississippi Doctor **25**:203 (Nov.) 1947. (*n*) Saunders, T. S.: The Use of Vioform in Local Dermatologic Therapy, Arch. Dermat. & Syph. **54**:456 (Oct.) 1946. (*o*) Sulzberger, M. B., and Kanof, A.: Comparative Evaluation of Preparations for the Prophylaxis and Treatment of Fungous Infections of Feet, U. S. Nav. M. Bull. **46**:822 (June) 1946.

3. Tate, B. C.: Principles of Treatment, in MacKenna, R. M. B.: Modern Trends in Dermatology, New York, Paul B. Hoeber, Inc., 1948, p. 355.

Other local and systemic measures were employed in special situations. Penicillin was administered when cellulitis, lymphangitis and lymphadenitis with fever were present; ultraviolet and roentgen irradiation, desensitizing procedures, starch baths, compresses and other therapeutic measures were used when they seemed desirable for a more complete or speedier treatment result. However, in each of the groups of diseases reported on some patients received diiodohydroxyquinoline therapy alone in order to serve as controls.

Moreover, "paired comparison" treatments [4] permitted a fair evaluation even in those patients who received adjuvant local or systemic therapy. Usually the "inert" vehicle was applied for comparison, but in some cases other active medicaments were incorporated in the vehicles to appraise the relative effectiveness.

In chronic and recurrent disease, e. g. sycosis vulgaris and dermatophytosis pedis, efforts were made to continue treatment for a prolonged period after clinical cure. Some patients were checked repeatedly for almost a year, and they remained free of lesions during that time while still on a certain measure of maintenance treatment.

RESULTS OF TREATMENT

Of the 150 patients treated with diiodohydroxyquinoline 66 had primarily infectious diseases (41 pyogenic and 25 fungous infections), 70 had primarily eczematous eruptions with secondary pyogenic infection and 14 had miscellaneous eruptions in which infection appeared to play little or no part.

Results of Treatment of Primarily Infectious Dermatoses.—In table 1 are shown the results for those with primarily infectious dermatoses. Forty-one of the 66 patients were clinically cured, 4 had no improvement and the remaining 21 patients showed some degree of improvement. Adjuvant therapeutic measures were seldom required in this group. These results indicate that diiodohydroxyquinoline has definite antibacterial and antifungal action. The antibacterial effect seems the more impressive, but this observation might prove erroneous when the results of larger treatment series are evaluated. Of greater importance is the fact that these good therapeutic results were obtained without a single instance of irritation or sensitization in the 66 patients in this group.

Results of Treatment of Secondarily Infected Dermatoses.—In table 2 are presented the results for patients with secondarily infected dermatoses. While 53 of the 70 persons were benefited by treatment, cures were few as compared with those obtained in the primarily infectious dermatoses (see table 1). In this group other topical therapeutic measures, usually of a "stimulating" character, had to be used frequently in the latter period of diiodohydroxyquinoline therapy or after treatment with diiodohydroxyquinoline had been stopped. This situation arose, generally, at a time when there was a clinical impression of freedom from secondary infection, e. g., disappearance of exudation,

4. Sulzberger, M. B.; Baer, R. L.; Kanof, A., and Lowenberg, C.: Methods for the Rapid Evaluation of the Beneficial and Harmful Effects of Agents Applied to the Human Skin, J. Invest. Dermat. **7**:227 (Oct.) 1946.

impetiginization and folliculitis in dermatitis venenata and seborrheic dermatitis and of fissuring in neurodermatitis. The small number of complete cures in primarily noninfectious dermatoses was not unanticipated, but the control of secondary pyogenic infection proved extremely valuable. This was particularly evident in infectious eczematoid derma-

TABLE 1.—*Results of Treatment of Primarily Infectious Dermatoses with Diiodohydroxyquinoline*

Diagnosis	No. of Cases	Cure	Improvement	No Improvement
Pyogenic infections				
Sycosis vulgaris *	16	13	3	0
Pustular folliculitis *	19	10	9	0
Impetigo contagiosa	3	3	0	0
Furuncles	2	0	1	1
Ecthyma	1	1	0	0
Total	41	27	13	1
Fungous infections				
Dermatophytosis pedis	17	8	7	2
Tinea cruris	6	6	0	0
Tinea corporis	2	0	1	1
Total	25	14	8	3
Total of pyogenic and fungous infections	66	41	21	4

* Differentiation of sycosis vulgaris and pustular folliculitis of the beard on clinical grounds alone is often difficult or impossible, the ultimate criterion being the histopathologic changes relative to the extension of the process along the follicle into the cutis. We used two criteria in our cases: (1) the duration of the disease and the frequency of recurrences and (2) the resistance of the infection to therapy.

TABLE 2.—*Results of Treatment of Secondarily Infected Dermatoses with Diiodohydroxyquinoline*

Diagnosis	No. of Cases	Cure	Improvement	No Improvement	Worse
Infectious eczematoid dermatitis	9	5	2	1	1
Nummular dermatitis	8	4	3	1	0
Dermatitis repens	1	0	1	0	0
Disseminate neurodermatitis	11	0	9	2	0
Seborrheic dermatitis	11	1	8	1	1
Dermatitis venenata	17	2	9	2	4
Miliaria rubra	2	2	0	0	0
Dermatitis medicamentosa	1	0	1	0	0
Eczematoid dermatitis	2	0	2	0	0
Pruritus ani et scroti	8	2	2	3	1
Total	70	16	37	10	7

titis, seborrheic dermatitis and nummular dermatitis, diseases well known for their resistance to treatment and for their irritability.

In this group it was again possible to confirm the low incidence of irritation and sensitization from diiodohydroxyquinoline. Only 6 of the 70 patients showed flare-ups in the course of diiodohydroxyquinoline therapy, some of them not until higher concentrations of the drug were used. Specific contact type sensitivity to diiodohydroxyquinoline was observed in 1 patient and was confirmed by the demonstration of

an eczematous type of patch test reaction, grade 2 to 3 to diiodohydroxyquinoline and grade 3 to 4 to iodochlorohydroxyquinoline; there were no reactions to control tests with ammoniated mercury, compound tincture of benzoin, benzoic acid and cinnamic acid. The patient had been admitted with a contact type dermatitis of the dorsa of the feet, and a patch test with the adhesive substance used in the shoe tongues gave a strongly positive reaction.

Results of Treatment of Miscellaneous Dermatoses.—In table 3 are presented the results for 14 patients with miscellaneous diseases of the skin in which the infectious element seemed unimportant. Obviously, in so small a group a quantitative evaluation of the results with diiodohydroxyquinoline has little significance.

Of course, no claim is made that cure of such diseases as rosacea, psoriasis and dermatitis herpetiformis can be obtained with any topical agent. However, improvement or complete clearing of the eruption for

TABLE 3.—*Results of Treatment of Miscellaneous Dermatoses with Diiodohydroxyquinoline*

Diagnosis	No. of Cases	Clearing	Improvement
Rosacea	10	7	3
Psoriasis	3	0	3
Dermatitis herpetiformis	1	0	1
Total	14	7	7

shorter or longer periods was observed and was maintained when the treatment was prolonged. Application of diiodohydroxyquinoline proved particularly beneficial in treatment of the macerated intertriginous lesions of psoriasis. Sulzberger and Baer [2a] referred particularly to the good results they obtained with iodochlorohydroxyquinoline in intertriginous psoriasis, and we have had the same experience with both iodochlorohydroxyquinoline and diiodohydroxyquinoline. In this group, application of diiodohydroxyquinoline caused no irritation and always produced some degree of improvement. In the light of the well known resistance of rosacea and intertriginous psoriasis to topical therapy, these results seemed very gratifying.

COMMENTS

We believe that our clinical results indicate that diiodohydroxyquinoline is an effective antibacterial and antifungal agent. The drug proved satisfactory not only in primary bacterial and fungous infections of the skin but also in secondarily infected dermatoses. The significance of secondary pyogenic infection in noninfectious dermatoses has probably never been given its full due, although it has been well dis-

cussed by others.[5] In such diseases as infectious eczematoid dermatitis, atopic dermatitis, seborrheic dermatitis, dermatitis venenata and some others, secondary pyogenic infection may be responsible for the persistence and spread of the original eruption. In our experience with diiodohydroxyquinoline control of the infectious element has often ameliorated the basic, noninfectious component of the eruption.

The clinical impression that diiodohydroxyquinoline has antibacterial and antifungal effect has been confirmed by various in vitro investigations of the quinolines.[6] However, it should be pointed out that in vitro observations of this type have no clinical validity until substantiated by actual therapeutic trial on the human skin. The test tube can in no way simulate the complex environmental, biologic and immunologic characteristics of the human skin, nor can it presage the incidence and severity of reactions that may be encountered.

Many drugs have been used in the treatment of pyogenic and fungous infections of the skin, and many have their individual proponents today. A cursory inventory was made of the drugs that were used at one time or other in the treatment of our group of patients: The list includes antibiotics, sulfonamides, bactericidal chemicals (ammoniated mercury, silver nitrate, potassium permanganate, iodine, sulfur, salicylic acid, tar, resorcinol and fatty acids) and dyes (methylrosaniline chloride, carbol-fuchsin, and acriflavine). It was our observation that diiodohydroxyquinoline was at least equal, and usually superior, to all these drugs from the therapeutic standpoint. Basic reviews of the effects of the various substances mentioned and some others were recently published by Pillsbury [5c] and by Combes and his collaborators.[7]

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5. (*a*) Stuart-Harris, C. H.: Bacteriology, in MacKenna, R. M. B.: Modern Trends in Dermatology New York, Paul B. Hoeber, Inc., 1948. (*b*) Stokes, J. H.: Fundamentals of Medical Dermatology, Philadelphia, University of Pennsylvania Press, 1942. (*c*) Pillsbury, D. M.: The Management of Bacterial Infection of the Skin, J. A. M. A. **132**:692 (Nov. 23) 1946. (*d*) Pillsbury, D. M.; Livingood, C. S., and Nichols, A. C.: Bacterial Flora of the Normal Human Skin: Report on the Effect of Various Ointments and Solutions with Comments on the Clinical Significance of This Study, Arch. Dermat. & Syph. **45**:61 (Jan.) 1942.

6. Jadassohn, W.; Pfanner, E., and Hausman, W.: Effects of Sterosan on Pathogenic Microorganisms in Vitro: Further Studies, Schweiz. med. Wchnschr. **77**:987 (Sept.) 1947. Albert, A.; Rubbo, S. D.; Goldacre, R. G., and Balfour, B. G.: Influence of Chemical Constitution on Antibacterial Activity: Study of 8-Hydroxyquinoline (Oxine) and Related Compounds, Brit. J. Exper. Path. **28**:69, 1947. Hirsch, J. and Desdogru, S.: Antistaphylococcal Effect of Penicillin, Streptomycin and 5,7-Dichloro-8-Hydroxyquinoline in Vitro, Arch. Biochem. **14**:213 (July) 1947.

7. Combes, F. C.; Zuckerman, R., and Bobroff, A.: Copper Undecylenate in the Treatment of Dermatomycoses, J. Invest. Dermat. **10**:477 (June) 1948.

Another important advantage of diiodohydroxyquinoline is its negligible tendency to irritate and sensitize. We believe that penicillin, sulfonamides, mercury, tars and sulfur—to name only the most frequently used agents—would have produced a much higher incidence of irritation and sensitization in our group of 150 patients. We encountered 6 instances of irritation and 1 of specific sensitivity in the 150 patients. It is important to note that all reactions occurred in the group of 70 patients with secondarily infected, irritable dermatoses and that not a single instance was encountered in the 66 patients with primary infections, even though many of these patients used the drug in high concentration for months. Furthermore, sensitization to diiodohydroxyquinoline has not the serious import of sensitization to antibiotics and sulfonamides, which may interfere with the subsequent administration of these vital drugs for serious systemic disease.

So far as comparison is possible from our own experience we prefer diiodohydroxyquinoline to iodochlorohydroxyquinoline for two reasons: (1) diiodohydroxyquinoline has caused less irritation and sensitization, even in concentrations up to 15 per cent, and (2) diiodohydroxyquinoline stains skin and clothes far less than does iodochlorohydroxyquinoline and is, therefore, much more acceptable to the patient.

Because of their extensive use in treatment of amebiasis and trichomonal infection the toxicity of the quinolines has been carefully investigated. Diiodohydroxyquinoline in particular, and also iodochlorohydroxyquinoline, was studied by David, Phatak and Zener [8] in experiments designed to elucidate the absorption and toxicity of the iodine radical after oral administration to guinea pigs, kittens and human beings. The authors concluded that the toxicity of these drugs is low in human beings. Basing their opinion on these results, Sulzberger and Baer [2a] stated the belief, relative to iodochlorohydroxyquinoline, that "there is no reason to fear toxic manifestations due to absorption." We observed no signs of iodism in any of our patients, even after prolonged use of the diiodohydroxyquinoline, and we are inclined to believe that the risk of systemic toxicity is small. However, the possibility must be remembered, especially since diiodohydroxyquinoline contains 63.9 per cent of iodine as compared with 41 per cent in iodochlorohydroxyquinoline. We agree with the recommendations that the iodinized quinolines should not be used over large areas for long periods and should not be used in treatment of dermatoses in which sensitivity to iodine is present.

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8. David, N. A.; Phatak, N. M., and Zener, F. B.: Iodochlorhydroxyquinoline and Diiodohydroxyquinoline: Animal Toxicity and Absorption in Man, Am. J. Trop. Med. **27**:29 (Jan.) 1944.

SUMMARY

Diiodohydroxyquinoline (5,7-diiodo-8-hydroxyquinoline), incorporated in ointments or lotions, was used in the topical treatment of 150 patients; the usual concentration was 3 per cent, but the drug was also employed in strengths varying from 1 to 15 per cent.

The chief topical effects of diiodohydroxyquinoline appear to be antibacterial and antifungal.

Diiodohydroxyquinoline was very effective in treatment of primarily infectious dermatoses and also in clearing up the infectious component of secondarily infected dermatoses.

Diiodohydroxyquinoline was well tolerated, even by highly inflammatory and irritable dermatoses. There was no irritation experienced among 66 patients with primary infections and 14 patients with certain noninfectious miscellaneous dermatoses. There were 6 instances of irritation and 1 of sensitization among 70 patients with secondarily infected, generally irritable dermatoses.

Treatment with diiodohydroxyquinoline cleared up eruptions that had resisted many other types of therapy, and it was our impression that the therapeutic effectiveness of this preparation was equal or superior to that of most other drugs used for similar conditions.

Dr. Irwin C. Winter, of G. D. Searle & Co., supplied the powdered diiodohydroxyquinoline (diodoquin®).

ENDEMIC OF INFECTION WITH MICROSPORUM AUDOUINI IN A FAMILY OF EIGHT PERSONS

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THE PRESENT article reports the unusual observation of infection with Microsporum audouini occurring in at least 7 members and probably in all 8 members of a family which included 2 adults.

EPIDEMIOLOGIC FEATURES

R., a boy 6½ years of age attending kindergarten at Roosevelt School in Union City, N. J., was found to have involvement of his scalp which was recognized early in January 1949 as being due to fungous infection.

By the latter part of February the entire family of 8 showed signs of infection, although it was not until mid-March that the father (aged 31) and daughter, K., (aged 4) reported to the health department. This family is of the low income group and lives in crowded quarters.

Inasmuch as not all the cases were of tinea capitis, the sequence of infection, age of the patients and location and a short description of the lesions are given in table 1.

SPECIAL REPORT OF A CASE

J., aged 5, presented fine scaling and thinning of the hair on several areas of the posterior aspect of the scalp. One week after the involvement of the scalp the left eyelid revealed a circinate lesion with scaly borders and central clearing. Examination by filtered ultraviolet light of the scalp and eyelash showed an emerald green fluorescence. There were three fluorescent hairs present in the midportion of the left upper eyelid. There was no edema nor any conjunctival inflammation. The organism was found on sodium hydroxide (10 per cent) preparation of one of these hairs. M. audouini was cultured from an eyelash as well as from the scalp.

From the Skin and Cancer Unit and the Department of Dermatology and Syphilology, Marion B. Sulzberger, M.D., chairman, Post-Graduate Medical School of New York University–Bellevue Medical Center.

1. Mrs. C. Lemmer, R.N., investigated the epidemiologic background in this case.

TABLE 1.—*Data on Eight Cases of Fungous Infection in One Family*

Name	Age	Location	Description
R.	6½	Scalp; right side of thorax	Discrete areas, dime sized to palm sized, over the entire scalp with some involvement of the occipital region; two rounded erythematous, slightly scaly lesions
J.	5	Scalp; left eyelid; left eyelash *	See special case report
B.	8	Posterior axillary line 2 inches (5 cm.) above the left iliac crest	Ring-shaped lesion with small papules and slight scaling
T.	7	Left shoulder; left thigh	Ring-shaped lesion with a clear center and erythematous border; smaller annular lesion
Father	31	Left forearm (extensor surface)	Quarter-sized, round, dry, erythematous, well defined lesion with slight scaling
K.	4	Upper portion of back	More than silver dollar–sized, circinate lesions with clearing centers and active borders
L.	1½	Right shoulder	Ring-shaped lesion with a clearing center and with papules on the border
Mother	31	Right infraclavicular area	Half dollar–sized, circinate lesion with central clearing and peripheral scaly border

* The great rarity of this localization has made it appear warranted to report the details of the case in the special case report.

TABLE 2.—*Laboratory Observations*

Name	Age	Examination with Wood's Light (Scalp or as Indicated)	Sodium Hydroxide Test	Culture for Microsporum audouini	Area Involved	Trichophytin Test Readings at:	
						15 Min.	48 Hr.
R.	6½	Positive	Not done Glabrous skin neg.	Positive Negative	Scalp; right side of thorax	Negative	Negative
J.	5	Positive; of eyelash also positive	Not done Eyelash positive	Positive Positive	Scalp; left eyelash	Negative	Negative
B.	8	Negative	Glabrous skin neg.	Positive	2 inches above iliac crest in left posterior axillary line	Negative	Negative
T.	7	Negative	Negative	Positive	Left shoulder	Negative	Negative
Father	31	Not done	Negative	Negative	Left forearm (extensor surface)	Not done	Not done
K.	4	Negative	Negative	Positive	Upper part of back	Negative	Negative
Mother	31	Negative	Positive	Positive	Right infraclavicular area	Negative	Negative
L.	1½	Negative	Negative	Positive	Right shoulder	Negative	Negative

RESPONSE TO THERAPY

All members of the family had received topical therapy with an ointment of unknown composition several months prior to their first visit to the clinic. This treatment had been employed for no longer than two weeks.

In from three to ten days while the patients were under our supervision, all the lesions except those situated on the scalp and eyelashes responded after the use of 5 per cent ammoniated mercury ointment.

In the 2 cases of tinea capitis treatment at first was with the topical medication zincundesal ("salundek," containing zinc undecylenate, 25 per cent; undecylenic acid, 2 per cent, and salicylanilide, 5 per cent, in a carbowax® base) but there was no improvement and roentgen epilation was necessary.

The patient with the infection of the eyelashes was treated by manual epilation.

COMMENTS

Absence of the organism in direct smears treated with sodium hydroxide in 4 of the cases with growth of M. audouini in parallel cultures are reported. It is usual to find fungi in the scrapings more readily than in cultures of material from the same sites. This significant reversal of the usual observations indicates the desirability of taking material for culture from all lesions suspected of being of fungous causation. In the reported series the peculiarity of there being positive cultures and negative direct smears may have been due to previous therapy.

The negative microscopic and cultural observations in the case of the father (31 years old) may be attributed to anti-fungus therapy. On clinical and epidemiologic grounds and in view of the response to therapy, it is considered highly probable that these lesions too were due to M. audouini.

The mother (31 years old) presented both a positive direct smear and a positive culture for M. audouini.

The relative facility of obtaining a response of all lesions of the glabrous skin to ammoniated mercury ointment has been demonstrated. To many investigators it may seem that M. audouini indicates recalcitrance to therapy. M. audouini per se is not resistant to local treatment when it is situated on the glabrous skin. The lesions on the scalp are difficult to manage, not because of resistance of the fungus to drugs but rather because its inherent nature leads to its growth and relative inaccessibility within the hair and hair follicle.

SUMMARY

The description is given of infection with M. audouini occurring in at least 7 and probably all 8 members of a family, including 2 (31 year old) adults, living closely together. The contagiousness and "anthropophilic"[2] nature of this fungus is again illustrated by the apparent ease of transmission and the negative reaction to trichophytin tests.

M. audouini was demonstrated in culture from the scalp in 2 cases and from the glabrous skin in 6 cases.

M. audouini infection of the eyelash was noted in 1 case.

2. Sulzberger, M. B.: Dermatologic Allergy: An Introduction in the Form of a Series of Lectures, Springfield, Ill., Charles C Thomas, Publisher, 1940, p. 272.

TREATMENT OF TINEA CAPITIS WITH ESTROGENIC HORMONES

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IT IS WELL known that fungous infections of the scalp tend to disappear spontaneously at about the time of puberty. Hormonal factors are most likely involved. This observation led to the use of an estrogenic substance in treatment of 11 patients by Lewis and Hopper in 1937.[1] Each patient received an injection at intervals of from three to seven days, the initial dose being 500 and subsequent doses being 1,000 international units. A total of 5,500 to 17,500 units was given. These authors were unable to observe improvement following this therapy.

Because of the close relation known to exist between the pituitary gland and the gonads and because the secretions from these glands are known to play an important role in the bodily changes at puberty, treatment by means of the anterior pituitary–like gonadotropic substance from the urine of pregnant women was given in four instances. The individual dose was approximately 200 rat units, and the total did not exceed 3,000 rat units. The patients did not experience improvement in their condition.

In 1946 Lewis, Hopper and Reiss [2] reported on a series of 23 patients infected with Microsporum audouini who had been treated with local applications of estrogenic and androgenic hormones. These hormones had seemed to be effective fungicides in the laboratory but were ineffective clinically. An ointment of petrolatum containing 1 mg. of diethylstilbestrol and 3 mg. of testosterone per gram was applied daily in 3 cases for many weeks. The immediate effect appeared to be loosening of the hair in 2 cases. In none of the cases did a cure result.

In 1941 Yáñez and associates [3] gave gonadotropic substance to 34 children with fungous infections of the scalp. The patients showed improvement after the fourth or fifth day. The scales disappeared; the diseased hair fell out, and the plaques cleared. The cure was usually

1. Lewis, G. M., and Hopper, M.: Ringworm of the Scalp: Clinical and Experimental Studies in Types of Infection Resistant to Treatment, Arch. Dermat. & Syph. **35**:466-470 (March) 1937.

2. Lewis, G. M.; Hopper, M. E., and Reiss, F.: Ringworm of Scalp: Clinical Data on Recent Cases; Experiences with Local Endocrine Therapy, J. A. M. A. **132**:62-65 (Sept. 14) 1946.

3. Yáñez, Weinstein; Brovo, and Guzman: Treatment of Ringworm of the Scalp with Gonadal Substances, Rev. méd. de Chile **69**:713-715 (Nov.) 1941.

complete on the tenth or twelfth day. These authors recorded only 3 failures. They reported no apparent difference in the result with the use of either male or female gonadotropic substance for persons of either sex.

Poth and Kaliski [4] in 1942 reported the treatment with estrogens of 30 patients with tinea capitis. Estrone was given orally in gelatin capsules, each containing 5,000 international units, 1 capsule daily. Local treatment consisted of the daily application of 1 Gm. of an ointment containing 5,000 international units of estrone. Most patients received combined oral and local medication. Each patient received orally 3 tablets (1 mg. each) of diethylstilbestrol daily, which was 75,000 international units daily, or 525,000 international units weekly. Most of this group used an ointment containing 125,000 international units per ounce (30 Gm.) in combination with oral therapy. Total doses of estrone varied from 14 to 56 capsules and from 7 to 56 Gm. of ointment; doses of diethylstilbestrol varied from 21 to 189 tablets and from 1 to 7 ounces (30 to 210 Gm.) of ointment. Only 4 patients failed to obtain a clinical cure.

Unfortunately, the articles by Yáñez and Poth did not indicate the number of cases due to infection with M. audouini. Infection with Microsporum lanosum and the "zoophilic" types of fungus will tend toward spontaneous cure, and almost any local therapeutic measure is likely to result in a cure.

Lewis and Hopper [5] used no treatment except the rubbing of petrolatum into the affected scalp and the washing of the scalp with a stiff brush. With this therapy they obtained as good results as with the use of any fungicidal application. All the patients had infections due to M. lanosum. The conclusions were that cure took place because the infected hairs fell out. The authors believed that the response was probably due to immunologic factors. Because of the perifollicular inflammation, epilation of the diseased hairs could be accomplished by rubbing.

Tinea capitis in 23 children was treated with gonadotropic hormones by Ghosh and Dey.[6] The hormones used were antuitrin®-S (anterior pituitary–like gonad-stimulating hormone from pregnancy urine), alpha estradiol (ovocylin®) and testosterone propionate (perandren®). The antuitrin® was used for both sexes; ovocylin,® for girls only, and perandren,® for boys. One cubic centimeter of the hormone preparation selected was given intramuscularly twice a week. An average of ten injections was given in five weeks.

4. Poth, D. O., and Kaliski, S. R.: Estrogen Therapy of Tinea Capitis, Arch. Dermat. & Syph. **45**:121-128 (Jan.) 1942.

5. Lewis, G. M., and Hopper, M. E.: Ringworm of the Scalp: Mechanism of Cure of Infections Caused by Microsporon Lanosum, Arch. Dermat. & Syph. **36**:1194-1196 (Dec.) 1937.

6. Ghosh, G. M., and Dey, N. C.: Studies in Ringworm: Therapy of Tinea Capitis by Gonadotropic Hormones, Indian M. Gaz. **80**:381-383 (Aug.) 1945.

It was found that the combination of hormone therapy and the daily local treatment gave better results than did the hormone therapy alone and that girls responded better than did boys and older children better than younger children. It was also found that a larger percentage of infections with M. audouini and Trichophyton crateriforme were cured than were those with Trichophyton violaceum. (T. violaceum may appear in adults, and infection with it probably is not related to gonadal activity.)

Previous to 1945 tinea capitis due of M. audouini was extremely rare in Georgia. Sixty-three cases of tinea capitis were seen in my private practice between the years 1940 and 1945. In 42 cases the infectious agent was M. lanosum; in 12 cases, Trichophyton gypseum; in 8 cases, Microsporum fulvum, and in only 1 case, M. audouini. Twenty-two cases were seen in 1945. Eight were due to M. audouini, 1 to M. fulvum, 9 to M. lanosum and 4 to T. gypseum. Thirty-eight cases were seen in 1946. Twenty-seven were due to M. audouini. Seventy-two of 88 cases seen in 1947 were due to M. audouini. The majority of the cases seen in 1948 and 1949 were also due to M. audouini.

It is apparent that M. audouini infection of the scalp was rare in Atlanta until war broke out and the causative fungus was spread in the South and elsewhere, with the countrywide change of residence of members of the armed forces and war workers. Infected children traveled from place to place with their parents and were responsible for epidemics of M. audouini infections in various cities. Secondary factors were overcrowding in children's institutions and a rapid turnover in these institutions, insufficient supervision, partly because of lack of personnel and equipment, and spread of infection through barber shops and theaters.

Numerous M. audouini infections were also seen and treated in the dermatologic clinics of Grady Memorial Hospital (Emory University School of Medicine, Dermatological Clinic, Herbert S. Alden, M.D., chief of service).

Various fungicides such as undecylenic acid, decupryl® solution [7] and salicylanilide were tried. Salicylanilide ointment was found to be the most efficient. In cases in which manual epilation was also done, the cure was accomplished in a shorter time. The greatest objection to manual epilation was the discomfort and pain associated with this procedure. Also, many of the hairs would break and eventually grow back infected, and then the painful procedure would have to be repeated.

Roentgen ray epilation was done in many cases. Although this seemed to be the treatment of choice, it could not be done in most cases

7. A solution of copper undecylenate 10 per cent and undecylenic acid 3 per cent in a low surface tension solvent containing equal parts of tetrachlorethylene and isopropyl alcohol, with dioctyl sodium sulfosuccinate as a wetting agent.

because of local prejudice and fear of this mode of therapy. Experimental work with hormone therapy for tinea capitis was done at the Grady Hospital dermatologic clinic, and some of these observations, as well as those made in private practice, my associates and I consider of sufficient value to report.

After the reports of Poth and Kaliski some patients with a zoophilic type of fungous infection were treated with diethylstilbestrol at Grady Memorial Hospital. In most cases there was a ready response to this treatment and no fluorescence was seen under the Wood light in four to five weeks. At that time this method seemed to show a slight improvement over the usual treatment. We considered our patients cured when no fluorescence was observed under the Wood light over a period of three months. In cases in which fluorescence was not a characteristic of the particular species of infection a negative culture was required as a criterion for cure.

During 1946 13 patients—8 boys and 5 girls—who had infection with M. audouini were treated with diethylstilbestrol administered locally and by mouth according to the dosage recommended by Poth and Kaliski. After eight weeks of treatment improvement was shown in only 3 cases. No infection was considered cured, but loosening of the hair was evident in 6 cases and manual epilation was done by the parent with much less discomfort to the patient. Then the local application was changed to that of undecylenic acid ointment, and after two to three months these 6 patients were considered as having cures. Tenderness and some discomfort of the breasts appeared in all 5 girls and in 2 of the boys. One girl manifested vaginal bleeding.

Estrogenic substance in the form of estrone ("theelin") was administered by injection in 12 cases of M. audouini infection. It appeared that the dose used by Lewis and Hopper was small. We started 6 patients with M. audouini infection on treatment with 2,000 international units given twice a week. In the sixth or seventh week the hair seemed to loosen but did not fall out spontaneously. These 6 patients showed improvement, but none had cures after twelve injections. The dose was gradually increased in 6 subsequent cases. The most effective dosage was found to be 10,000 to 20,000 international units once a week for six weeks. With this dosage the hair would loosen usually after the second or third injection but again showed no tendency to fall out spontaneously.

Of the 12 patients 9 were boys and 3 were girls. The ages ranged from 6 to 11. One of the boys who had a generalized infection failed to show sufficient loosening of the hair after twelve weeks of treatment, and his scalp was epilated with roentgen rays. Two of the 3 girls complained of swelling and soreness in their breasts, and administration of the hormones was discontinued after the fourth and sixth injection. Both of these patients were treated with roentgen ray epilation.

One patient showed improvement after eight weeks but did not return for further treatment. After twelve weeks of hormonal treatment 6 patients were treated further by manual epilation and local applications of salicylanilide ointment. The manual epilation was not painful as compared with that in cases in which the patients had never received injections of estrogenic hormones. The manual epilation was done by the parent at home and also at the clinic. After manual epilation was started the clearing of the scalp was much more rapid. In 1 case within two weeks the hair showed no more fluorescence under the Wood light. The longest period of treatment was sixteen weeks. The average time for cure in the 6 cases, after manual epilation was started, was seven weeks.

Fifty-six persons with tinea capitis due to M. audouini were treated with estrogenic hormones in my office and followed for at least three months. The estrogenic substances (water insoluble) used were solution amniotin® in oil (each cubic centimeter containing natural estrogens, derived from gravid mares' urine, equivalent in terms of estrone to 20,000 international units, 2.0 mg. crystalline estrone) and solution "estrusol" in oil (peanut oil containing 20,000 units per cubic centimeter principally of estrone, with small amounts of other natural estrogens, from pregnant mares' urine preserved with chlorobutanol, 0.5 per cent). The dose was 1 cc. (20,000 units of amniotin® or 20,000 units of "estrusol") and was given subcutaneously or intramuscularly at weekly intervals. Rarely more than six doses were given, although in 4 cases the patients were given ten injections each. The results with the two preparations were about the same. The youngest child was 4 years of age, and the oldest, 10. Most of the children were between the ages of 6 and 9. Thirty-four of these patients had been treated previously with some form of local medication with little or no response. The average length of treatment in these cases before the hormone therapy was tried was two and one-half months.

PROCEDURE

As shown in the accompanying table, the average age of our patients was 7.5 years. The infected hair usually became loosened after the third or fourth injection. At this time the parent was asked to purchase a purple X bulb (Westinghouse, 250 watts), or a portable hand Wood filter glass apparatus (Black Light Products), and an epilating forceps. Instructions were given for removing the fluorescent hairs. In some cases, patches of fluorescent hairs were outlined with ink on the patient's head and the parent would pull out all hairs that were loosely attached. The purple X bulb was found useful to many parents in detecting the fluorescent hairs. Although the fluorescence was not as clear and satisfactory as that observed with the Wood light, the economy of the bulb made it accessible to the average patient. The parent was cautioned not to allow the bulb to overheat because this

might cause it to burst. When colored glasses were worn by the person performing the manual epilation, the hairs would appear more clearly and the light would not tire the eyes as much. A few parents preferred to buy the portable hand Wood filter glass apparatus. Whenever the hair was epilated the head was shampooed immediately afterward and salicylanilide ointment applied. The stocking cap and the usual precautions and instructions for patients with ringworm of the scalp were used.[8] Manual epilation was to be done daily, and the child was checked and given further injections at weekly intervals. The average number of injections was 6.4. In cases in which the infection was not widespread the successful manual epilation of infected hair could be accomplished in a few days. In extensive cases the progress was slower and many hairs were not removed properly and would again grow back fluorescent. In mild cases a cure was accomplished in as short a time as three to four weeks. The infected hair remained loose for about three weeks after the last injection. If there continued to be fluorescence

Treatment with Estrogenic Hormones and Manual Epilation of Tinea Capitis Caused by Microsporum Audouini

	No. of Patients	Age	Average No. of Injections	Average No. of Injections Before Loosening of Hair	Average No. of Weeks Before Negative Results on Wood Light Examination	No. Cured	No. Improved	No. for Which Treatment Failed
	8	5	6.5	5	11.5	7	1	0
	6	6	6.5	3	8.5	4	0	2
	24	7	6.3	3	9.5	21	1	2
	6	8	5.8	3	11.4	6	0	0
	6	9	6.3	5	11	3	1	2
	6	10	7.2	4	12	3	1	2
Totals	56	7.5	6.4	3.8	10.6	44 (78.6%)	4 (7.1%)	8 (14.3%)

under the Wood light after sixteen weeks but there was considerable improvement, the patient's condition was considered improved. If the hair failed to loosen or improvement was only slight after twelve weeks of treatment the treatment was considered a failure. Cases in which treatment failed were not included when the percentages were computed for the table for the columns headed "Average Number of Injections Before Loosening of Hair" and "Average Number of Weeks Before Negative Results on Wood Light Examination." The hair of patients for whom hormone treatment failed was epilated with roentgen rays.

With exclusion of the cases in which there was improvement or failure of treatment, our statistics revealed that cures resulted in 78.4 per cent of the cases in an average time of 10.6 weeks. These results evidenced an advancement in the therapy of cases of tinea capitis in which roentgen rays were not used.

COMMENT

The hair in M. audouini infections usually is firmly attached and cannot be removed with ease. When pulled with tweezers manually the hair breaks off near the scalp, thus preventing satisfactory manual epila-

8. Dobes, W. L.: Ringworm of the Scalp: An Epidemic in Georgia, J. M. A. Georgia **36**:259-263 (July) 1947.

tion, but with treatment with the estrogenic hormones, in most cases, the hair becomes loose and successful epilation with forceps is facilitated. In this manner the administration of an estrogenic hormone becomes a useful adjuvant treatment in cases in which local treatment and manual epilation are preferred.

The estrogenic hormones were most useful in treating the boys. The majority of the girls acquired swelling and soreness of the breasts which, although temporary, caused sufficient discomfort to the patient and worry to the parents that it was thought wise not to use this treatment in girls. Fortunately, the M. audouini infection occurs three times as frequently in boys as in girls.

Administration of testosterone propionate was tried in both boys and girls, but the results were not encouraging, especially in the girls. Two of 6 boys showed some loosening of the hair. Three girls showed no improvement or loosening of the hair. Twenty-five milligram doses were given twice a week for four weeks. The testosterone did not seem to stimulate males sexually or otherwise, nor did any of the patients show any ill after effects.

The optimum dosage of estrogenic substance seemed to be 10,000 to 20,000 units at weekly intervals. Children less than 6 years of age were given 10,000 units, and those over 6 years of age, 20,000 unit doses, although this scale varied in some children who were physically light or heavy for their average age. As previously stated, the hair would usually become loosened after the third injection. Some children showed loosening of the hair after the first injection, and others, not until after the fourth or fifth. If loosening did not occur after the fifth injection, it rarely did so after further treatment. After our optimum dosage was determined it was our practice not to give more than six injections at weekly intervals. In a few of the early cases as many as eight or nine, and even twelve, injections were given. After three years we had not seen any ill effects from this treatment. If loosening of the hair does not appear after six injections, failure can be expected, and therefore further treatment with hormones is not advisable. Theoretically some depression of growth might be expected if the treatment should be of long duration.

In 6 patients, along with the loosening of the hair, the bright green fluorescence changed to a dull gray fluorescence. In these cases the manual epilation was not important because the fungus apparently had died and the hair gradually was shed and replaced with normal hair. One can consider cure as resulting in these cases with injections of hormones alone. Among the cases of M. audouini infections in which estrogenic hormones were given by injection, cures were indicated in only 9 per cent of those in which manual epilation was not used.

The fact that M. audouini rarely affects adults has been explained as being due to some structural change in the hair produced by the gonadal activity at puberty. S. Rothman and co-workers[9] reported results of investigations on the chemical composition and potency against fungi of adult hair fat and its fractions. The authors concluded that immunity of the adult scalp to M. audouini infection depends on the presence in sebaceous secretion of a fungistatic concentration of certain fatty acids. Rare cases in adults may be due to deficient sex hormone secretion, resulting in an infantile type of sebum. Spontaneous cure apparently depends on sterilization of the skin adjacent to and lining the follicular skin surface. Natural shedding of the hair results in removal of all infected hairs over a period of many months. Infection of new hairs is prevented by the fungistatic adult type of hair fat.

Sufficiently large doses of estrogenic hormones apparently stimulated a temporary production of an adult type of sebum, which with some structural changes caused loosening of the already infected hair, thus allowing it to shed and be removed with ease.

SUMMARY AND CONCLUSIONS

Thirteen patients with M. audouini infection of the scalp were treated with diethylstilbestrol. In no cases did cure result, but in 6 cases there was loosening of the hair enabling painless manual epilation.

Sixty-eight persons were treated with injections of estrogenic hormones. Fifty-six of these patients were followed closely. The hair in most cases had loosened sufficiently after the third and fourth injections to enable painless manual epilation. Salicylanilide ointment was used locally. Cures resulted in 78.6 per cent of the cases in an average of 10.6 weeks.

Estrogenic hormones are considered a worthwhile adjuvant therapy in cases in which local treatment is preferred to roentgen ray epilation.

The treatment is suitable only for males, because of frequent reactions, especially in the form of swelling and painful breasts, in females.

The optimum dosage appears to be 10,000 to 20,000 international units of estrogenic substance given subcutaneously once a week for six weeks.

Manual epilation of the loosened infected fluorescent hair is essential for early and successful treatment.

If loosening of the hair does not appear after six injections further treatment with hormones usually is unsuccessful and theoretically not advisable.

514 Doctors Building.

9. Rothman, S.; Smiljanic, A.; Shapiro, A. L., and Weitkamp, A. W.: The Spontaneous Cure of Tinea Capitis in Puberty, J. Invest. Dermat. **8**:81-98 (Feb.) 1947.

DERMATITIS CAUSED BY DDT

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IT IS NOTEWORTHY that in spite of the almost worldwide use of DDT (2,2-bis[*p*-chlorophenyl] 1, 1, 1-trichlorethane) very few untoward reactions caused by it have been reported. Even during the Italian campaign in December 1943 and January 1944, when it was used extensively on all the troops of the United States Army for the destruction of body lice to control a louse-born typhus epidemic in Naples, not only was the measure so effective that not 1 case of typhus occurred in an American soldier but as a matter of fact and consternation there was no mishap or unpleasant reaction.[1]

To evaluate subclinical manifestations of possible poisonous effects Case [2] undertook an ingenious study. He placed 2 volunteer men in contact, for two forty-eight hour periods, with the walls of a chamber coated with a film containing 2 per cent DDT by weight and covered by a thin film of oil. The men wore only shorts. The temperature and the humidity of the chamber were raised to induce sweating.

These exposures caused chiefly subjective symptoms: mental irritability, apprehensiveness, tiredness, the feeling of heaviness, aching in bones and joints, the feeling of incompetence and extreme distaste for exertion of any kind.

Further there occurred a pronounced but transitory fall in blood pressure, indicanuria and an increase in the number of siderocytes from a normal of 3 to 6 to 18 to 20 per thousand. The number of reticulocytes increased from 16 to 20 per thousand to 36 to 40. The blood picture became normal after twenty-six days. The results of this study suggest that the siderocyte level might serve as a useful index in the diagnosis of obscure cases of DDT poisoning.

Niedelman[3] and later Stryker and Godfroy[4] reported independent instances of dermatitis which might have been caused by DDT. It was

1. Ahnfeldt, A. L.: DDT Powder for Destruction of Body Lice, J. Tennessee M. A. **37**:263-265 (Aug.) 1944.

2. Case, R. A. M.: Toxic Effects of 2,2-*bis* (*p*-chlorophenyl) 1,1,1-Trichlorethane (D.D.T.) in Man, Brit. M. J. **2**:842-845 (Dec. 15) 1945.

3. Niedelman, M. J.: Contact Dermatitis Due to DDT, Occup. Med. **1**:391-395 (April) 1946.

4. Stryker, G. V., and Godfroy, B.: Dermatitis Resulting from Exposure to DDT: Preliminary Report, J. Missouri M. A. **43**:384-386 (June) 1946.

Leider,[5] however, who was first to report a case of dermatitis of unquestioned authenticity. It occurred in a fireman who acquired a generalized eczematous dermatitis on the face, upper part of the trunk and the flexor surfaces of the extremities a week after he had used a spray containing DDT. Patch tests with this spray and also with a 5 per cent solution of DDT in acetone (which caused no dermatitis in 50 "control" subjects) caused 4+ and 3+ reactions respectively in this patient. Further, Leider gave the following reasons for his contention that this patient presented a true instance of allergic eczematous contact type dermatitis caused by DDT: 1. There was a known exposure. 2. An adequate period (one week) for incubation intervened between exposure and appearance of the dermatitis. 3. The clinical picture was that of typical eczematous dermatitis usually presenting a prolonged course.

I too have treated a patient who presented a clinical picture and course similar in most respects to those in the case reported by Leider.

REPORT OF A CASE

On Aug. 4, 1949, J. H. D., a 64 year old executive, consulted me on account of an extensive and angry-appearing dermatitis which affected the anterior surfaces of his body; mainly the face, neck, chest, upper part of the abdomen and flexor surfaces of the arms. At the perimeter of the dermatitis and even on some distant parts of the body a pinpoint macular herald rash resembling miliaria was present.

The dermatitis itself was deep red and edematous, with a few areas of necrosis on the chest wall. The tissues on the neck were swollen so much out of proportion that they were on a line with the cheeks. Serum exuded over the entire area of dermatitis. The patient complained of intolerable itching, burning and pain.

He stated that about the middle of July there had appeared an area of dermatitis on the upper portion of his chest. Shortly thereafter some degree of swelling had developed. As the process increased, burning and itching ensued.

He consulted a dermatologist on the third or the fourth day. A diagnosis of miliaria was made. He was given roentgen irradiation, and calamine lotion was applied. During the following three weeks the intensity and the extent of the dermatitis increased in spite of semiweekly treatments with roentgen radiation. The discomfort was severe.

The extraordinary features the patient presented were (1) a dermatitis of great intensity, (2) a menacing edema of the neck, (3) a distressing character of the subjective symptoms, (4) an elevation of temperature to 103 F., (5) a tendency toward the delineation of the dermatitis to the anterior surface of the body and (6) a miliaria-like herald rash extending peripherally.

A clinical diagnosis of cellulitis (erysipelas) was the most likely except for the slow development. A detailed history, which reconstructed the period prior to the very start of the dermatitis, gave the clue for the most likely cause. (Later, when it was safe, I was able to verify this.) During the first week of July it was exceptionally warm and humid. The patient recalled that on one occasion, about

5. Leider, M.: Allergic Eczematous Contact-Type Dermatitis Caused by DDT, J. Invest. Dermat. **8**:125-126 (March) 1947.

July 4, to cool himself he had lain prone and without a shirt outdoors on the lawn. It had been sprayed heavily with DDT about that time as a precaution against flies and other insects.

Course and Treatment.—On August 4 my first problem was to combat the erysipelas-like cellulitis. This was successfully accomplished through intramuscular injections of 40,000 units of aqueous solution of penicillin at four hour intervals for a period of four days. Ice cold compresses of a saturated solution of boric acid were applied continuously during this period.

On August 8 all the alarming symptoms disappeared. The patient was permitted out of bed. Areas of residual dermatitis were covered with zinc oxide paste N. F. Since the patient still experienced itching he was given chlorothen (tagathen®), 25 mg. every four hours.

On August 15 areas of residual dermatitis were still present; the administration of zinc oxide paste and chlorothen was continued. There were still some areas of dermatitis on August 29. Treatment as before was continued.

On October 28 there were still occasional episodes of flare-up on the previously involved areas of dermatitis but of minimal quality. I considered it safe to make a patch test on the patient with a 5 per cent solution of DDT in acetone. On October 29 the reaction to the patch test was intensely positive.

SUMMARY

A case of dermatitis of major severity and lengthy duration caused by DDT is described.

It was interesting to observe the great similarity of this case to the case described by Leider.

The paucity of true instances of DDT-caused dermatitis is worthy of especial comment.

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RETICULUM CELL SARCOMA

Report of a Case, with Comment on Its Genesis

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THIS IS the report of a case of reticulum cell sarcoma involving the skin and testes, with fatal outcome after a duration of one year. Lymph nodes were not primarily affected, although later the inguinal nodes were involved secondarily by extension from the testicular lesions. Permission for autopsy was not obtained, but physical and roentgenologic examinations revealed no other lymph node enlargement. Clinically the lesions resembled those of mycosis fungoides d'emblee or Spiegler-Fendt sarcoid. Histologically, the earlier biopsies showed a picture consistent with that described for Spiegler-Fendt sarcoid, while later ones of specimens from testes and skin revealed changes typical of reticulum cell sarcoma.

This observation raises the question of the correlation between the clinical and the histologic picture of the lymphoblastomas involving the skin primarily. In 1902, Breakey,[1] referring to the cutaneous manifestations of the lymphoid diseases, stated that "while the study of these dermatoses has been prosecuted with greater vigor than ever within the last few years, and a large number of valuable contributions made to the literature of these forms of disease of the skin, there is still a great deal of diversity of opinion in the classification of different cases." The situation since has changed little. Since the cause or causes of these diseases are unknown, the need for a classification based on cytologic structure of the lesions has been expressed by various authors.[2]

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1. Breakey, W. F.: A Case of Mycosis Fungoides, J. Cutan. Dis. **20:** 316 (June) 1902.

2. (*a*) Gall, E. A., and Mallory, T. B.: Malignant Lymphoma: A Clinicopathologic Survey of Six Hundred and Eighteen Cases, Am. J. Path. **18:** 381 (May) 1942. (*b*) Klemperer, P.: The Relationship of the Reticulum to Diseases of the Hematopoietic System, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman, New York, International Press, 1932, vol. 2, pp. 655-671. (*c*) Hellwig, C. A.: Malignant Lymphoma, Am. J. Clin. Path. **16:**564 (Sept.) 1946.

Ewing [3] made the following statement: "The complexities of the subject of lymphoid tumors depend chiefly upon the lack of knowledge of etiology and partly upon lack of anatomical classification."

Roulet,[4] in 1930, under the name of "Retothelsarkom" described a group of tumors arising from lymphatic tissue. He believed that they were derived not from lymphatic cells but from reticulum cells of lymphatic tissue. In the classification of Ewing,[3] reticulum cell sarcoma is synonymous with large cell lymphosarcoma. Such a classification was used by other authors, including Ormsby and Montgomery,[5] Sugarbaker and Craver [6] and Eller.[7] The term lymphosarcoma was originally introduced by Kundrat,[8] who described the growth as a tumor which arose not from a single node but from a group of nodes or from lymphoid tissue of a mucous membrane and which, after remaining localized for an indefinite period, spread either by direct extension or through the lymphatics. Use of the term lymphosarcoma was, however, objected to by many investigators,[9] including Gall and Mallory,[2a] who expressed the belief that "such a segregation is artificial and merely represents a phase in the course of the disease."

Knowledge concerning the reticulum was first obtained through the discovery by Tigri,[10] in 1853, of a network of stellate cells forming the framework of the splenic pulp. Shortly thereafter this reticulum of cells and fibrils was found to exist in lymphatic as well as in splenic tissue. The similarity between the reticulum cells of the embryonal spleen and

3. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 386-433.

4. Roulet, F.: Das primäre Retothelsarkom der Lymphknoten, Virchows Arch. f. path. Anat. **277**:15, 1930.

5. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, p. 873.

6. Sugarbaker, E. D., and Craver, L. F.: Lymphosarcoma: A Study of One Hundred and Ninety-Six Cases with Biopsy, J. A. M. A. **115**: 17 (July 6) 1940.

7. Eller, J. J.: Tumors of the Skin: Benign and Malignant, Philadelphia, Lea & Febiger, 1939, pp. 463-469.

8. Kundrat, H.: Ueber Lympho-Sarkomatosis, Wien. klin. Wchnschr. **6**:211, 1893.

9. Gibbons, H. W.: The Relation of Hodgkin's Disease to Lymphosarcoma, Am. J. M. Sc. **132**:692 (Nov.) 1906. Flashman, D. H., and Leopold, S. S.: Leukosarcoma, with Report of a Case Beginning with a Primary Retroperitoneal Lymphosarcoma and Terminating with Leukemia, ibid. **177**:651 (May) 1929. Baldridge, C. W., and Awe, C. D.: Lymphoma: A Study of One Hundred and Fifty Cases, Arch. Int. Med. **45**:161 (Feb.) 1930. Brunschwig, A., and Kandel, E.: A Correlation of the Histologic Changes and Clinical Symptoms in Irradiated Hodgkin's Disease and Lymphoblastoma of Lymph Nodes, Radiology **23**:315 (Sept.) 1934.

10. Tigri, A.: Nuova disposizione dell'apparecchio vascolare sanguigno della milza umana, Gazz. med. ital. feder. tosc. **3**:17, 1853.

those of the adult spleen was clearly pointed out by Klemperer.[2b] Not only is this similarity morphologic, but also the cells possess the same developmental potentialities. Each is capable of differentiation along four lines, with the formation of hematic, phagocytic, endothelial and fibroblastic cells. The reticulum of lymphoid and myeloid tissue can, according to Klemperer, who cited Maximow, be considered "an embryonal germinal layer of the adult organism."

Foot [11] stated that more difference of opinion exists concerning the diagnosis of reticulum cell sarcoma than concerning that of almost any other type of lymphoid neoplasm. He expressed the opinion that the reason for this might lie in the fact that "there are two distinct branches of the reticulum cell family; that resident in the lymph follicles and that found in the areolar connective tissue. Some pathologists will not admit that a reticulum cell sarcoma can arise in the latter situation, calling such tumors fibrosarcomas." However, Maximow,[12] as a result of animal experimentation and tissue culture, concluded that cells with the same developmental potentialities as the reticulum cells have are scattered throughout the body. In the skin these cells, which he called undifferentiated mesenchymal cells, are perivascular. These primitive cells have also been referred to as lymphoidocytes,[13] primitive blood cells,[14] hemocytoblasts,[15] histioblasts [16] and common lymphoid stem cells.[2a] Perhaps most frequently they have been designated as reticulum cells.[17] The nature of the primitive reticulum cell is well summarized in the statement by Ehrlich and Gerber [18] that "there has been accumulated a convincing array of evidence to substantiate the view that

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11. Foot, N. C.: Classification and Diagnosis of Lymphoid and Allied Tumors, New York State J. Med. **42**:2220 (Dec.) 1942.

12. Maximow, A. A., and Bloom, W.: A Textbook of Histology, ed. 3, Philadelphia, W. B. Saunders Company, 1938, pp. 52-53.

13. Pappenheim, A.: Atlas der menschlichen Blutzellen, Jena, G. Fischer, 1912.

14. Farrar, G. E., Jr., and Cameron, J. D.: Monocytic Leukemia with Data on the Individuality and Development of the Monocyte, Am. J. M. Sc. **184**:763 (Dec.) 1932.

15. Turnbull, H. M.: The Anatomy of Erythropoiesis, in Vaughan, J. M.: The Anemias, ed. 2, London, Oxford University Press, 1936, p. 11.

16. Ferrata, A.: Le Emopatie, Milan, Soc. ed. libraria, 1918, pt. 1.

17. (*a*) Klemperer.[2b] (*b*) Ewing.[3] (*c*) Roulet.[4] (*d*) Sugarbaker and Craver.[6] (*e*) Edling, L.: Contribution to the Pathology and Clinical Picture of Reticulum Cell Sarcoma, Radiology **30**:19 (Jan.) 1938 (*f*) Callender, G. R.: Tumors and Tumor-like Conditions of the Lymphocyte, the Erythrocyte and the Reticulum Cell, Am. J. Path. **10**:443 (July) 1934. (*g*) Herbut, P. A.; Miller, F. R., and Erf, L. A.: The Relation of Hodgkin's Disease, Lymphosarcoma, and Reticulum Cell Sarcoma, Am. J. Path. **21**:233 (March) 1945.

18. Ehrlich, J. C., and Gerber, I. E.: The Histogenesis of Lymphosarcomatosis, Am. J. Cancer **24**:1 (May) 1935.

the cytoplasmic reticulum present throughout the body, in the spleen, lymph nodes, liver, bone marrow, and perivascular tissues, retains in adult life the multipotency of embryonal mesenchyme."

As pointed out by Klemperer,[2b] various investigators have observed the steps in the transformation of the reticulum cell into the lymphocyte in the embryo, in tissue culture and in the adult. The concept of a widely distributed multipotent primitive mesenchymal cell (reticulum cell) which, as the result of certain stimuli, acts as a lymphoid stem cell best explains the nature and histologic structure of those conditions which are generally included among the lymphoblastomas. The classification proposed by Gall and Mallory [2a] is based on the tumor's predominant cell, each cell type being recognized as representing a stage in the development of the lymphocyte from the reticulum cell. They divided the malignant lymphomas into seven groups, as follows:

1. Stem cell lymphoma
2. Clasmatocytic lymphoma
3. Lymphoblastic lymphoma
4. Lymphocytic lymphoma
5. Hodgkin's lymphoma
6. Hodgkin's sarcoma
7. Follicular lymphoma

The stem cell lymphoma corresponds to the reticular and intermediate types of lymphosarcoma described in detail by Ehrlich and Gerber.[18] The reticular type consists primarily of nuclei dispersed in a cytoplasmic syncytium without any clear cell boundaries. The nuclei are very large, 10 to 12 microns in diameter, oval, usually vesicular, with a moderately thick, darkly staining nuclear membrane which is frequently infolded. Mitotic figures are observed frequently and are usually of normal configuration. One to three nucleoli are present. In the intermediate type, the cellular constituents are partly in syncytial arrangement and partly discrete. According to Gall and Mallory,[2a] the fundamental similarity between these types is so great that their separation into two distinct entities is not justified. Varying numbers of lymphocytes and monocytes are observed in these tumors, and the fibrillar reticulum is comparatively sparse.

The second constituent of the reticulum cell sarcoma group in this classification by Gall and Mallory, the clasmatocytic lymphoma, has as its predominant cell the clasmatocyte or monocyte. This cell is described as being smaller than the stem cell but distinctly larger than the lymphocyte, with pronounced phagocytic properties. Hellwig [2c] suggested that the classification would benefit by the removal of the clasmatocytic lymphoma from the reticulum cell sarcoma group since the cells making up the tumor are not actually primitive reticulum cells but rather have

differentiated from them and have taken on the function of pronounced phagocytosis. They expressed the opinion that the clasmatocytic lymphoma should be classified as monocytoma.

When the clasmatocytic lymphoma is made a distinct entity, the stem cell lymphoma remains as the reticulum cell sarcoma. As regards the remaining five classifications, the lymphoblastic lymphoma is characterized by the predominance of the lymphoblast. In lymphocytic lymphoma the lymphocyte is the predominant cell. In the follicular lymphoma the lymphocyte is again the predominant cell but the tumor is characterized by a distinct type of architecture, with the normal lymph node structure replaced by multiple follicle-like nodules of varied size. The nature of Hodgkin's disease has been and will be the subject of much discussion. If the view is accepted that it is a primary malignant tumor, it may be considered to be derived from the reticulum cell, since the pathognomonic Reed-Sternberg cell is probably a reticulum cell which has become large and multilobed or multinucleated.[2a] Hodgkin's sarcoma has also been the subject of much controversy. Callender [17f] and Richter [19] maintain that it and reticulum cell sarcoma are identical. Whether or not one accepts the existence of Hodgkin's sarcoma per se, the evidence at hand indicates that this growth too is derived from the reticulum cell.

Transformation from one type of lymphoma to another may occur. Numerous reports on such changes have appeared. Gall and Mallory [2a] found that in 23.2 per cent of their cases of malignant lymphoma repeated biopsies revealed a change in histologic structure toward less differentiation. Hellwig [2c] found that 20 per cent of his cases showed a change toward less differentiation, with 80 per cent retaining the original histologic structure. Herbut and associates [17g] reported 6 cases which histologically showed various transformation between Hodgkin's disease, reticulum cell sarcoma and what these authors described as lymphosarcoma. It is believed, therefore, that all malignant lymphomas are derived from one source, the reticulum cell, and that the development of a given form or the transformation from one type to another depends on unknown stimuli acting on this cell.

REPORT OF A CASE

P. P., a 67 year old white man, was first admitted to Bellevue Hospital on April 16, 1948. The present illness had begun six months previously with development of a growth on his left cheek. This was followed by gradual appearance of other tumors on his face. He denied previous cutaneous disease or pruritus. His past history was essentially noncontributory except that he had had a fracture of the right leg in 1934 and recurrent ulcers of that extremity.

Physical examination revealed a well developed, well nourished 202 pound (92 Kg.) man not acutely ill. On his face were ten firm, nontender, elevated,

19. Richter, M., in discussion on Foot.[11]

rounded, well defined reddish brown tumors varying from 2 to 10 cm. in diameter (fig. 1). Most of the lesions were circular. Some telangiectases were present overlying the larger lesions. No lymph node enlargement was detected. The liver and spleen were not palpable. No nasopharyngeal tumors were observed. Examination of the heart and lungs failed to disclose any abnormalities. Blood pressure was normal, 130 systolic and 86 diastolic. Both legs, particularly the right, had areas of brownish pigmentation and chronic dermatitis; several large ulcers were present on the lower third of the right leg. Pulsation of neither the dorsalis pedis nor posterior tibial arteries could be felt. The tentative clinical diagnoses were mycosis fungoides d'emblee and arteriosclerotic ulcers of the right leg. During this period of observation the patient's general condition remained good and no new tumors appeared.

Fig. 1.—Photograph taken in April 1948 of lesions of the face: firm, nontender, elevated, rounded, reddish brown nodules varying from 2 to 10 cm. in diameter.

On May 31 the patient left the hospital against advice and was not seen again until July 20. The difference between his general condition in July and that on his departure from the hospital was striking. There was loss of weight of approximately 60 pounds (27 Kg.); the patient was much less alert, answered questions poorly and slept much of the time. On this admission two scrotal masses were noted. These were smooth, firm and nontender and could not be transilluminated. Aspiration failed to yield any fluid. The patient stated that these masses had appeared about the same time as had those on the face. Presumably they had been overlooked during his first admission. Because of large ulcers of the right leg and foot which failed to respond to therapy, an amputation of the right leg at midthigh was done. At the same time a bilateral orchiectomy was done. The remainder of the body was essentially the same as during his first admission except for some change in the cutaneous lesions. Many of those seen on the first admission were still present although larger. Depressed smooth scars marked the sites

of those which had responded to therapy. Many new tumors were observed on the face, left thigh, leg and foot. Some of the tumors on the foot had broken down to form a large ulcer. About three weeks after the orchiectomy, recurrence of the scrotal masses occurred. During the period of hospitalization these masses were seen to extend to both inguinal regions with involvement of the lymph nodes in these areas. Repeated examinations failed to reveal enlargement of any other lymph nodes, the spleen or the liver. New tumors continued to appear on the face and left lower extremity. These were pink at the onset, later becoming reddish brown and finally bluish red. During the week prior to death some of the tumors became purpuric and crusted (fig. 2). Aside from one lesion which appeared on the right stump there was no cutaneous involvement other than that on the face and left lower extremity. The disease ran a gradual downhill course, and the patient died on Oct. 29, 1948, approximately one year after the onset of his illness.

Fig. 2.—Photograph taken in October 1948 of lesions of the face, showing purpura and crusting of some of the nodules.

Laboratory Studies.—Repeated examinations of the blood the last three days before death revealed a consistently normal white blood cell count. The amount of hemoglobin varied between 8.0 and 12.5 Gm. per hundred cubic centimeters, and the erythrocyte count fluctuated between 3,090,000 and 3,700,000 per cubic millimeter. Determinations of nonprotein nitrogen, total protein, albumin-globulin ratio, icterus index, cephalin flocculation, chlorides, sugar, cholesterol, acid phosphatase and alkaline phosphatase were repeatedly within normal limits. Frequent urinalyses yielded normal results. The Mazzini serologic test for syphilis gave a negative reaction. Roentgenographic studies of the gastrointestinal tract, skull, vertebral column, pelvis, extremities and chest all showed essentially normal conditions.

Histologic Studies.—In a biopsy specimen from a tumor of the cheek taken on April 17, 1948 (fig. 3), the overlying epidermis was flattened and thinned. Below was a narrow zone of normal corium. The rest of the corium and the hypoderm were occupied by anastomosing ovoid and irregular masses of dense

cellular infiltrate, closely grouped in the upper portion but more discrete and separated in the lower; here the cells were more loosely aggregated. Pilosebaceous follicles and sweat glands were caught in the infiltrate. Around and within some of these foci were irregular clumps of fragmented elastic fibers showing basophilic degeneration; also a number of distorted degenerated nuclei were present. Collagen bundles were broken into small irregular clumps or had completely disappeared.

Scattered in irregular fashion throughout the nodules of infiltrate were cells of several types. There were lymphocytes, rounded or irregular from compression,

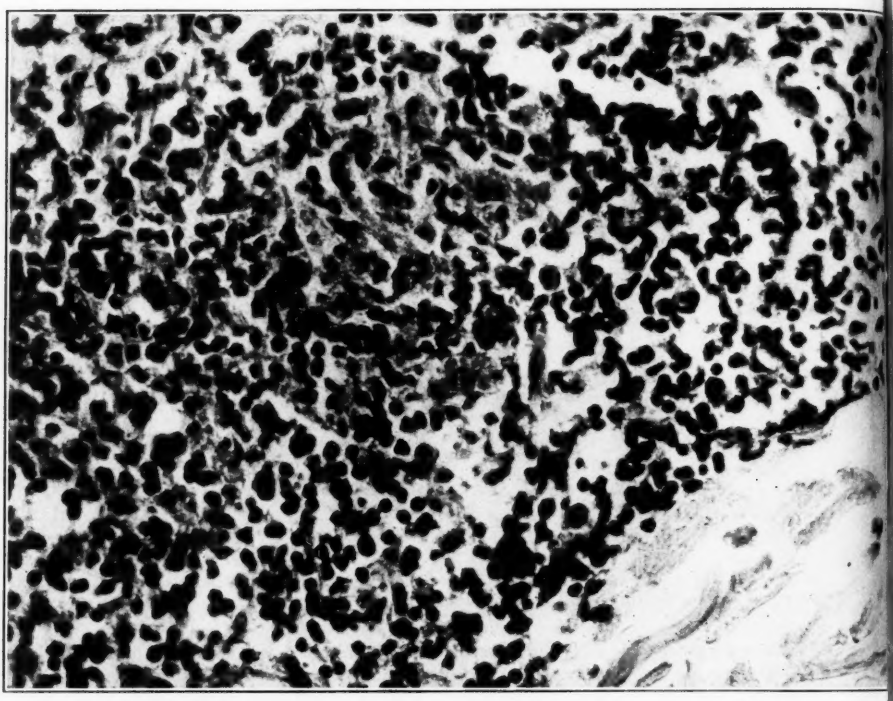

Fig. 3.—Biopsy specimen taken April 17, 1948, from a tumor of the cheek. High power view (× 515) showing nature of infiltrate: chiefly lymphocytes and histiocytic type cells, the latter greatly in the minority.

small or large, with a rim of pinkish cytoplasm; and cells with large, irregular, pale-staining vesicular nuclei, a few indented, and having relatively large amounts of pale eosinophilic cytoplasm of irregular outline, some showing syncytial connections with similar neighbors, and containing ingested debris. There were cells with similar nuclei but poorly defined cytoplasm; some were very deeply stained while others showed pyknosis or karyorrhexis. A very rare mitotic figure was seen. These were epithelioid cells, histiocytes and reticulum cells. Capillaries were present throughout the infiltrate. In the upper portion of the section there were more signs of necrosis and phagocytosis than in the lower part.

In brief, the histologic picture resembled that of Spiegler-Fendt sarcoid. In a biopsy specimen taken from a lesion on the chin on April 29 (figs. 4 and 5), the general picture resembled that of the previous specimen, but the cellular infiltrate was denser, more confluent and extended more deeply. The connective tissue had almost completely disappeared except for a thin subepidermal zone. The resemblance to Spiegler-Fendt sarcoid was even greater since the cells of the infiltrate were predominantly lymphocytes, histiocytes, epithelioid cells and deeply staining histiocytes (reticulum cells), the latter now more numerous and prominent. Mitoses were still rare. A silver stain (Wilder) for reticulum showed the presence

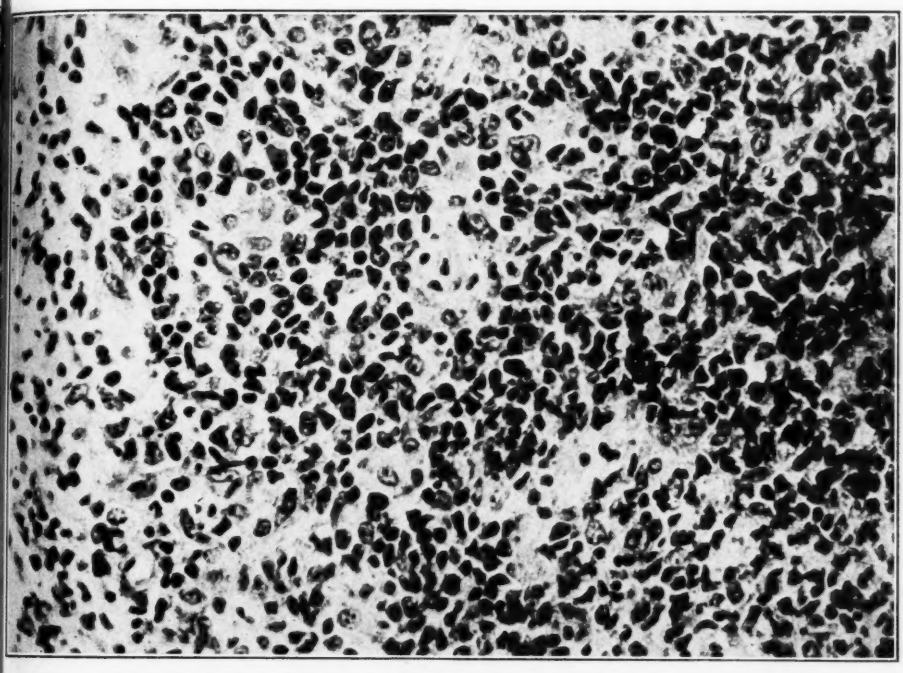

Fig. 4.—Biopsy specimen taken April 29, 1948, from a lesion on the chin. High power view (× 501) showing increase in histiocytic type cells (reticulum cells), the lymphocytes and other inflammatory cells having decreased in number.

of a meshwork of fine fibrils around individual cells or groups of two or three cells.

In a biopsy specimen taken from a scrotal tumor on August 17, seven sections of both testicles showed an extensive malignant tumor which had all but effaced every remnant of normal testicular tissue. In a few places there were isolated epididymal glands and vestiges of the tunica albuginea, tunica vaginalis and spermatic cord. No seminiferous tubules were identified. The tumor was characterized by growth of large masses of undifferentiated cells with few identifying characteristics. These cells showed a moderate degree of pleomorphism, particularly in shape and staining characteristics. Only scanty stroma had been elaborated,

so that thin fibrils separated small clusters of cells from each other. However, there was no distinctive pattern. Large portions of the growth had become necrotic, and much hemosiderin had been deposited. The growth was poorly vascularized. The predominant cell type had a nucleus about twice the size of a small lymphocyte and was rather deeply stained and vesicular. These nuclei were round, oval or slightly indented; only a few were in mitosis. They resembled the immature cells seen in the germinal centers of lymphoid follicles. They had almost no distinguishable cytoplasm and no distinct cell membrane. The growth differed from the usual carcinoma and embryonal carcinoma of the testis in that it was bilateral, lacked both alveolar and papillary structures, pseudotubercles and

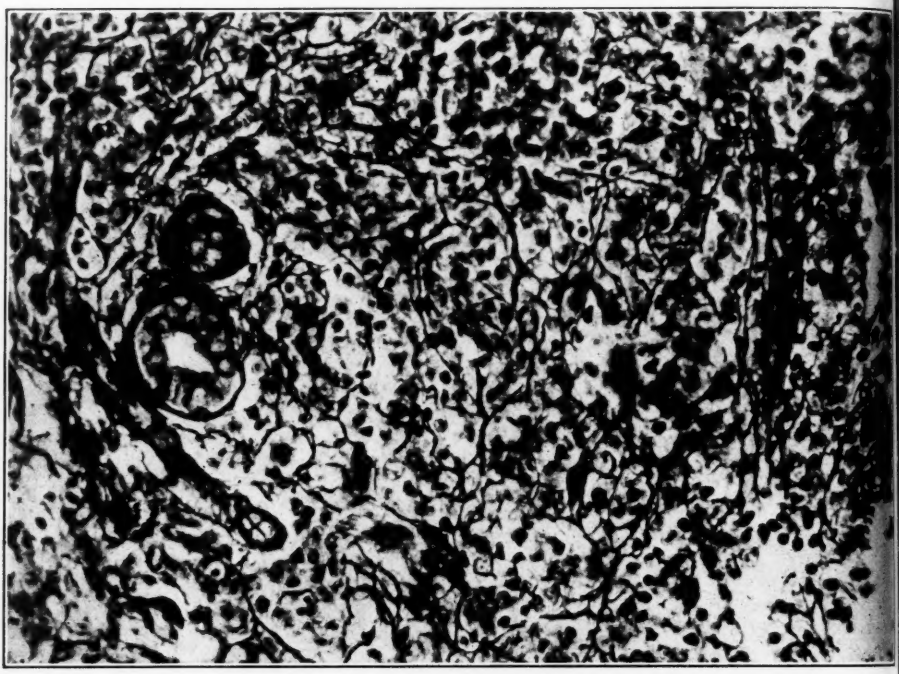

Fig. 5.—Biopsy specimen taken April 29, 1948, from a lesion on the chin. Wilder silver stain for reticulum showing presence of profuse delicate reticulum (× 509).

lipid-rich cytoplasm and lacked the usual double cell type with the small lymphocytic cell types interspersed between cells with large vesicular nuclei. The tumor cells were considerably smaller and the nuclei were less vesicular than in the characteristic cell of seminoma. Furthermore, no teratomatous elements were present.

The foregoing description and the diagnosis of reticulum cell sarcoma were made by Dr. William C. Von Glahn, director of the Department of Pathology of Bellevue Hospital, and his associates.

In a biopsy specimen taken from a tumor of the left thigh on September 4 (fig. 6), the epidermis was thinned and compressed by a very dense massive

cellular infiltrate which filled the entire corium and invaded the hypoderm, infiltrating the fat lobules. The cells of the infiltrate consisted almost entirely of reticulum cells. They had no clearly definable cytoplasm, and the nuclei were of the histiocytic type, vesicular but deep staining, large and varied in size and shape, and containing one to three nucleoli. Mitotic figures and degenerated forms were numerous, with signs of growth predominating. A few lymphocytes and an occasional neutrophil were scattered about. The general appearance was that of an actively growing tumor, and the picture resembled that of the infiltrate in the testes. The tumor was clearly recognizable as a reticulum cell sarcoma.

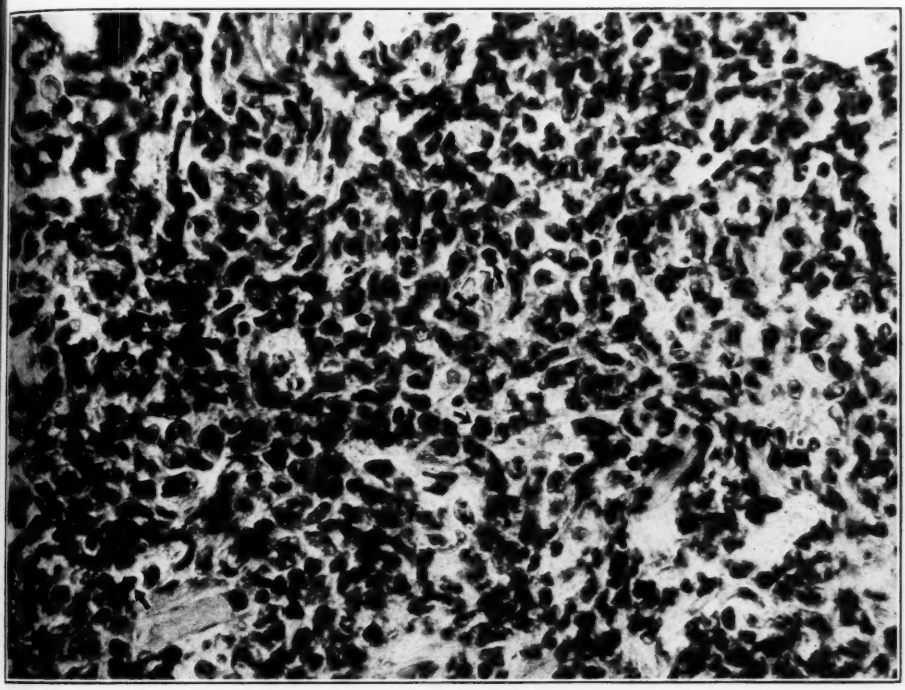

Fig. 6.—Biopsy specimen taken Sept. 4, 1948, from a tumor of the left thigh. High power view (× 519) showing preponderance of reticulum cells, with arrows pointing to the many mitotic figures in a single field. Only a few lymphocytes are present, and the appearance is clearly that of a rapidly growing tumor.

Treatment.—During the first period of hospitalization certain of the tumors were treated with grenz rays while others were exposed to roentgen rays. There was not any favorable therapeutic response to the former except for involution of one small nodule. The lesions treated with roentgen rays received a total dose of 400 to 1,200 r unfiltered at 100 kilovolts. There was partial to complete regression of those which received the greater amount of radiation. After the second admission, one facial tumor was treated with a total dose of 1,400 r at 200 kilovolts with filtration of 0.5 mm. of copper and 1.0 mm. of aluminum.

Two other lesions were treated with a total dose of 2,400 r at 140 kilovolts with the same filtration. There was about 50 per cent involution of the three tumors. One month later a course of combined roentgen irradiation and administration of nitrogen mustard (methyl-bis [2-chloroethyl] amine hydrochloride) was started. One tumor was given six daily exposures of 50 r at 140 kilovolts with filtration of 0.25 mm. of copper and 1.0 mm. of aluminum. With use of these same factors, another tumor was given the 300 r dose at one time. On each of the following eight mornings the patient received an intravenous injection of 0.05 mg. of nitrogen mustard per kilogram of body weight. Within one hour after the injection a third tumor was exposed to 50 r and a fourth tumor to 300 r. No side effects were noted from this therapy. The following observations were made: Nodules untreated by radiation were not influenced; nodules treated with small doses of radiation just prior to the administration of nitrogen mustard were not affected; nodules treated with small doses of radiation and nitrogen mustard concurrently were not affected, and nodules treated with large doses of radiation and nitrogen mustard concurrently regressed, with the effect no greater than that which might be expected from large doses of radiation alone. On the basis of these observations and also the appearance of a new tumor on the right thigh during the period of its administration, it was concluded that administration of nitrogen mustard had been of little value in the treatment of this patient and that irradiation was the method of choice.

COMMENTS

Because of the lack of postmortem studies, it is impossible to state definitely that there was not any visceral involvement in our patient. However, clinical observation, roentgenographic studies and other laboratory tests make it appear likely that lesions were limited to the skin, testes and inguinal lymph nodes. The latter involvement occurred as a result of direct extension of the testicular tumors. Whether the cutaneous lesions appeared first, to be followed shortly by the testicular tumors, or whether the sequence was reversed is difficult to say. According to the history the two manifestations appeared about the same time. Whatever the sequence, it is not necessary to postulate a spread from one site to the other via the lymphatics or blood. Since the reticulum cell is not, as was originally considered, limited to the spleen and lymph nodes, "we do not need to explain generalized tissue changes as the result of embolization or metastases, but may regard them as local proliferations of mesenchymal cells." [20]

Numerous reports made it clear that a close relation exists between mycosis fungoides and the malignant lymphomas. Fraser [21] reported 2 cases of mycosis fungoides which terminated in reticulum cell sarcoma. Wile and Stiles [22] reported a case of mycosis fungoides which subse-

20. Robb-Smith, A. H. T.: The Reticular Tissue and the Skin, Brit. J. Dermat. **56**:151 (July-Aug.) 1944.

21. Fraser, J. F.: The Interpretation of Mycosis Fungoides as a Variety of Lymphosarcoma, Arch. Dermat. & Syph. **11**:425 (April) 1925.

22. Wile, U. J., and Stiles, F.: Clinical Mutations in Lymphoblastomas, J. A. M. A. **104**:533 (Feb. 16) 1935.

quently developed into Hodgkin's disease. Montgomery and Watkins [23] reported 2 cases of monocytic leukemia which at one time presented the clinical picture of mycosis fungoides. Robb-Smith [20] noted that the transformation of mycosis fungoides d'emblee into reticulum cell sarcoma is not unlikely. Ormsby and Montgomery [5] observed that in many cases of clinical mycosis fungoides d'emblee histologic examination showed that the condition actually was a lymphosarcoma or other type of lymphoblastoma. Goldsmith [24] pointed out the difficulty in certain cases in differentiating between mycosis fungoides, Hodgkin's disease and reticulum cell sarcoma. Wertheim and Smith [25] recently reported the case of a patient with clinically characteristic mycosis fungoides whose biopsy sections showed different histologic pictures. A small, young cutaneous nodule showed an infiltrate which was considered to be almost entirely of the reticulum cell type; the larger and older nodule had greater pleomorphism and was considered more typical of mycosis fungoides. Observations by Symmers [26] led him to express the belief that mycosis fungoides is neither a clinical nor a pathologic entity but rather a form of Hodgkin's disease or lymphosarcoma. Berman [27] stated that the clinical diagnosis of mycosis fungoides might correspond to different pathologic entities within the lymphoblastoma group. Klemperer [2b] and Fraser [21] maintained that the cells of the cutaneous lesions of mycosis fungoides are derived from the primitive mesenchymal cells of the skin, which are identical with the reticulum cells of the spleen and lymph nodes.

Lewis,[28] from study of his own 4 cases and a review of the literature, concluded that clinical differentiation of Spiegler-Fendt sarcoid "from granuloma fungoides d'emblee, lymphogranulomatosis, lymphosarcoma and the leukemias, when observed in an atypical form may be difficult." Histologically he described the reticulum cells seen in Spiegler-Fendt sarcoid as similar in appearance to those observed in mycosis fungoides and other lymphoblastomas. Trimble,[29] in reporting a case of Spiegler-

23. Montgomery, H., and Watkins, C. H.: Monocytic Leukemia: Cutaneous Manifestations of the Naegeli and Schilling Types; Hemocytologic Differentiation, Arch. Int. Med. **60**:51 (July) 1937.

24. Goldsmith, W. N.: The Reticuloses, Brit. J. Dermat. **56**:107 (May-June) 1944.

25. Wertheim, L., and Smith, G. S.: Mycosis Fungoides, Arch. Dermat. & Syph. **57**:625 (April) 1948.

26. Symmers, D.: Lymphoid Diseases, Arch. Path. **45**:73 (Jan.) 1948.

27. Berman, L.: Pathological Nature of Mycosis Fungoides, Arch. Path. **29**:530 (April) 1940.

28. Lewis, G. M.: Is Spiegler-Fendt Sarcoid a Clinical or Histologic Entity? Arch. Dermat. & Syph. **31**:67 (Jan.) 1935.

29. Trimble, W. B.: Sarcoid (Spiegler-Fendt Type), Arch. Dermat. & Syph. **7**:666 (May) 1923.

Fendt sarcoid, pointed out that a similar histologic picture had been seen in cases of lymphosarcoma. Bowen,[30] in an article entitled "Mycosis Fungoides and Sarcomatosis," pointed out the similarity between the former condition and Spiegler-Fendt sarcoid. Lewis, commenting on a case presented by Templeton [31] as lymphosarcoma, expressed the opinion that Spiegler-Fendt sarcoid could not be ruled out. Sweitzer [32] and Lewis [28] concluded that Spiegler-Fendt sarcoid should be considered one of the lymphoblastomas.

The clinical and histopathologic observations on our patient lead us to the opinion that Spiegler-Fendt sarcoid is not a specific entity and should be dropped as a histologic and clinical diagnosis. It represents clinically a nodular eruption of the skin not preceded by other forms of dermatitis and thus has the appearance of mycosis fungoides d'emblee (forme fruste). Histologically it may represent the earlier phases of reticulum cell sarcoma or other lymphoblastoma. In view of the long duration of older recorded cases, other unknown or unrecognized diseases may have been involved. The tendency today is toward a belief that all diseases grouped as lymphoblastomas, even if not due to the same cause, produce histopathologic changes in which the essentially diseased cells are the primitive mesenchymal reticulum cells and their developmental derivatives. These primitive cells are widely spread throughout the body, so that other tissues such as the skin may give rise to a primary focus of disease, and the condition need not arise primarily from lymph nodes or blood-forming tissues.

The treatment of reticulum cell sarcoma has consisted primarily, of surgical procedures or irradiation. Gall [33] reported 9 cases of stem cell lymphoma in which treatment was by complete surgical excision with a median duration of survival of five years. Hellwig [34] reported 2 cases in which treatment was by radical surgery, the patients living and remaining free of disease for twenty and ten years respectively. Jackson [35] stated that "if reticulum cell sarcoma is localized to an accessible region, excise very widely and hope for the best." Holmes and

30. Bowen, J. T.: Mycosis Fungoides and Sarcomatosis, J. Cutan. & Genito-Urin. Dis. **15**:65 (Feb.) 1897.

31. Templeton, H. J.: Lymphoblastoma (Lymphosarcoma?), Arch. Dermat. & Syph. **25**:726 (April) 1932.

32. Sweitzer, S. E.: Sarcomatosis Cutis of Spiegler, Arch. Dermat. & Syph. **11**:481 (April) 1925.

33. Gall, E. A.: The Surgical Treatment of Malignant Lymphoma, Ann. Surg. **118**:1064 (Dec.) 1943.

34. Hellwig, C. A.: Malignant Lymphoma: The Value of Radical Surgery in Selected Cases, Surg., Gynec. & Obst. **84**:950 (May) 1947.

35. Jackson, H. J., Jr.: The Practical Aspects of the Diagnosis, Treatment and Prognosis of Hodgkin's Disease and Allied Disorders, Radiology **50**:481 (April) 1948.

Schulz [36] reported on 2 patients with stem cell lymphoma who had had single lesions at the time of radiation therapy and who were alive and free of disease more than five years after the last treatment. They pointed out also that no long survivals occurred in patients with multiple lesions. Apparently a localized reticulum cell sarcoma aggressively treated offers a better prognosis than one in which multiple lesions are already present before treatment is started. In the case of generalized disease irradiation has been employed primarily as a palliative measure.

The administration of nitrogen mustard appeared promising in the treatment of generalized reticulum cell sarcoma. Eichenlaub and Olivo [37] reported on a patient so treated in whom regression of cutaneous and visceral lesions occurred. However, the patient died from a toxic reaction caused by the drug. Goodman and associates [38] noted encouraging results in the treatment of lymphosarcoma. Osborne and co-workers [39] reported on a patient with lymphosarcoma whose condition was improved by administration of nitrogen mustard but who died twelve days afterward from pneumonia following agranulocytosis; at autopsy there was no evidence of lymphosarcoma. Other investigators [40] concluded that the use of nitrogen mustard offered little in the treatment of reticulum cell sarcoma except for palliative effect when irradiation had failed or was contraindicated. In our case greater effectiveness of roentgen irradiation was demonstrated.

SUMMARY

A case is reported of reticulum cell sarcoma of the skin and testes with fatal outcome after a duration of one year, in which the earlier specimens from skin nodules resembled the picture seen in so-called Spiegler-Fendt sarcoid but in which later specimens proved the condition to be a reticulum cell sarcoma.

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36. Holmes, G. W., and Schulz, M. D.: Radiation Treatment of Localized Malignant Lymphoma, New England J. Med. **235**:789 (Nov. 28) 1946.

37. Eichenlaub, F. J., and Olivo, M. A.: Nitrogen Mustard Therapy of Lymphosarcoma: Report of a Case, M. Ann. District of Columbia **17**:391 (July) 1948.

38. Goodman, L. S.; Wintrobe, M. M.; Dameshek, W.; Goodman, M. J.; Gilman, A., and McLennan, M. T.: Nitrogen Mustard Therapy, J. A. M. A. **132**:126 (Sept. 21) 1946.

39. Osborne, E. D.; Jordan, J. W.; Hoak, F. C., and Pschierer, F. J.: Nitrogen Mustard Therapy in Cutaneous Blastomatous Disease, J. A. M. A. **135**:1123 (Dec. 27) 1947.

40. Craver, L. F.: Lymphomas and Leukemias: The Value of Early Diagnosis and Treatment, J. A. M. A. **136**:244 (Jan. 24) 1948; The Nitrogen Mustards: Clinical Use, Radiology **50**:486 (April) 1948. Rhoads, C. P.: Nitrogen Mustards in the Treatment of Neoplastic Disease, J. A. M. A. **131**:656 (June 22) 1946.

A review of the literature suggests that reticulum cell sarcoma may arise not only from the reticulum cells of lymph nodes but also from primitive multipotent mesenchymal cells elsewhere, including the skin. It is believed that different developmental stages of this type of cell are seen in the different types of lymphoblastomas. We believe that our case illustrates the autonomous development of a reticulum cell sarcoma in the skin and that so-called Spiegler-Fendt sarcoid is merely a phase in its histopathologic development.

Nitrogen mustard therapy was ineffective. Roentgen ray therapy was effective but only palliative.

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EOSINOPHILIC GRANULOMA OF THE SKIN

Report of Cases Representing the Two Different Diseases Described as Eosinophilic Granuloma

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EOSINOPHILIC granuloma of the skin has been since 1946 a frequently discussed topic in the American dermatologic literature.[1] At first a good deal of confusion prevailed since entirely different cutaneous lesions were described under this diagnosis; recently, however, it has become apparent that the cutaneous lesions described under the term eosinophilic granuloma can be divided into three groups, namely (1) cases associated with and identical in pathogenesis with eosinophilic granuloma of the bone, (2) cases characterized by torpid, asymptomatic, purplish patches on the face and (3) a heterogeneous group of cases having in common nothing but a large percentage of eosinophils in a granulomatous infiltrate.

From the Department of Dermatology, Harvard Medical School, and the Dermatologic Service, Massachusetts General Hospital, Dr. Chester N. Frazier, chief.

1. (*a*) Buley, H. M.: Eosinophil Granuloma of the Skin, J. Invest. Dermat. **7**:291, 1946. (*b*) Weidman, F. D.: The "Eosinophilic Granulomas" of the Skin, Arch. Dermat. & Syph. **55**:155 (Feb.) 1947. (*c*) Lewis, G. M., and Cormia, F. E.: Eosinophilic Granuloma: Theoretic and Practical Considerations Based on the Study of a Case, ibid. **55**:176 (Feb.) 1947. (*d*) Lever, W. F.: Eosinophilic Granuloma of the Skin: Its Relation to Erythema Elevatum Diutinum and Eosinophilic Granuloma of Bone; Report of a Case, ibid. **55**:194 (Feb.) 1947. (*e*) Curtis, A. C., and Cawley, E. P.: Eosinophilic Granuloma of the Bone with Cutaneous Manifestations: Report of a Case, ibid. **55**:810 (June) 1947. (*f*) Laymon, C. W., and Sevenants, J. J.: Systemic Reticuloendothelial Granuloma: Comparison of Letterer-Siwe Disease, Schüller-Christian Disease and Eosinophilic Granuloma, ibid. **57**:873 (May) 1948. (*g*) McCreary, J. H.: Eosinophilic Granuloma with Simultaneous Involvement of Skin and Bone, ibid. **58**:372 (Oct.) 1948. (*h*) Lever, W. F.; Lane, C. G.; Downing, J. G., and Spangler, A. S.: Eosinophilic Granuloma of the Skin: Report of Three Cases, ibid. **58**:430 (Oct.) 1948. (*i*) Pinkus, H.; Copps, L. A.; Custer, S., and Epstein, S.: Reticulogranuloma: Report of a Case of Eosinophilic Granuloma of Bone Associated with Nonlipid Reticulosis of Skin and Oral Mucosa Under the Clinical Picture of Hand-Schüller-Christian Disease, Am. J. Dis. Child. **77**:503 (April) 1949. (*j*) Cobane, J. H.; Straith, C. L., and Pinkus, H.: Facial Granulomas with Eosinophilia: Their Relation to Other Eosinophilic Granulomas of the Skin and to Recticulogranuloma, Arch. Dermat. & Syph. **61**:442 (March) 1950.

The third group, on account of its varying etiology, does not deserve the diagnostic term eosinophilic granuloma. However, elimination of this group still leaves two entirely different diseases endowed with the same diagnostic term.

In this paper, 1 case of the first type and 2 cases of the second type of eosinophilic granuloma of the skin will be described and the differences in the clinical and histologic picture of these two diseases will be pointed out.

REPORT OF CASES

CASE 1.—*Cutaneous lesions associated and identical with eosinophilic granuloma of the bone.*

A white boy aged 19 months was admitted to the Massachusetts General Hospital on May 1, 1948. He had had a normal birth and had developed normally until, when he was 6 months old, both external ear canals began to drain. When he was 9 months of age a papular eruption was first noted about the ears. This eruption soon spread throughout the scalp and appeared on the trunk.

Examination on admission revealed the child to be in fairly good general health. The scalp was erythematous and covered with thick scales and yellowish crusts extending to the hair line. The chest, abdomen, groins, axillas and midscapular area showed a diffuse eruption composed of innumerable closely set, brownish red, hyperkeratotic, scaling papules. On the lower part of the abdomen and in the groins the papules had coalesced and were in part covered by crusts. No definite diagnosis was made from the clinical appearance of the cutaneous lesions, but Darier's disease was considered most likely. Both ear canals were filled with exudate and granulation tissue. The cervical, left occipital, left axillary and inguinal lymph nodes were considerably enlarged, nontender and firm.

Course of the Disease.—On May 7 a simple mastoidectomy and aural polypectomy were performed on the right side. It was noted that the tympanic membrane was perforated. The entire mastoid bowl was filled with granulation tissue which had eroded through the posterior-superior bony canal wall and filled the middle ear. The horizontal semicircular canal was identified, and the incus was seen embedded in granulation tissue. No removal of granulation tissue from the middle ear was attempted. On May 28 a simple mastoidectomy was performed on the left side. The observations were the same as they had been on the right side except that the posterior bony canal wall was intact. A slight purulent discharge from the ears persisted. The patient left the hospital on June 24.

The patient was readmitted on July 10 because of an increase in the purulent discharge from the ears and the reappearance of large polyps in the external ear canals. The lesions on the trunk had at that time almost completely involuted; but erythema, scaling and large crusts were still present throughout the scalp. The cervical and inguinal lymph nodes were as prominent as they had been at the time of the first admission. Granulation tissue was again removed from the ear canals on August 2. On August 23, 24 and 25 three roentgen treatments were given to both mastoid areas. Each treatment consisted of 150 r, at 200 kilovolts and 20 milliamperes, with a filtration of 0.25 mm. of copper and 1 mm. of aluminum. The patient was discharged from the hospital on the day of the last roentgen treatment. Within the next two weeks the discharge from the ears gradually lessened and finally ceased.

On September 24 the boy reentered the hospital because of an enlarging lesion above the left ear at a site which previously had shown persistent crusting. The lesion consisted of a tender, soft, heavily crusted tumor measuring 5 by 6 cm. in

diameter and raised 1.5 cm. above the level of the skin (fig. 1). On removal of the crust bright red, easily bleeding granulomatous tissue was visualized. The boy's general condition was good. No discharge was noted from the ears. On October 8 the lesion above the ear was treated by roentgen irradiation. The dosage was 200 r, at 200 kilovolts and 20 milliamperes, with a filtration of 0.25 mm. of copper and 1 mm. of aluminum. By the end of October 1948 the lesion had healed.

Laboratory Data.—The Hinton test of the blood for syphilis gave negative results. Results of several urinalyses were normal. White blood cell counts ranged from 4,600 to 13,400. The hemoglobin was 9.4 Gm. An erythrocyte count was 4,260,000. Repeated differential blood counts were normal, with the number of eosinophils varying from 0 to 4 per cent. The serum cholesterol content was 179 mg. per hundred cubic centimeters. The reaction to the tuberculin test was negative at a dilution of 1 : 1,000. Roentgenologic examination of the chest showed normal pulmonary fields. Roentgenograms of the mastoid processes showed increased density bilaterally. No destruction of bone was noted, but there was

Fig. 1 (case 1).—Appearance of the granulomatous tumor above the left ear.

some decalcification in the right petrous bone. Roentgenograms of the skull and entire skeleton showed normal conditions.

Histologic Examination.—Three specimens were available for histologic examination.

A specimen obtained from the skin of the chest showed a thickened horny layer which was in part parakeratotic and permeated with numerous polymorphonuclear leukocytes (fig. 2*A*). The rete malpighii was thin. The rete pegs were absent in some places but elongated in others. A bandlike infiltrate was present in the upper part of the corium in close apposition to the epidermis, invading it in many areas. The cells of the infiltrate in most areas lay separated from each other in an edematous stroma but in a few areas were closely packed. The great majority of the cells were histiocytes characterized by large, pale, irregularly shaped, often indented nuclei and abundant cytoplasm (fig. 2*B*). A few of the histiocytes showed mitotic figures. Eosinophils and lymphocytes were scattered through the infiltrate in small numbers. The capillaries within the infiltrate were dilated, and in a few areas extravasated erythrocytes were noted. The lower part of the corium was normal except that some of the sweat glands were surrounded by a histiocytic infiltrate.

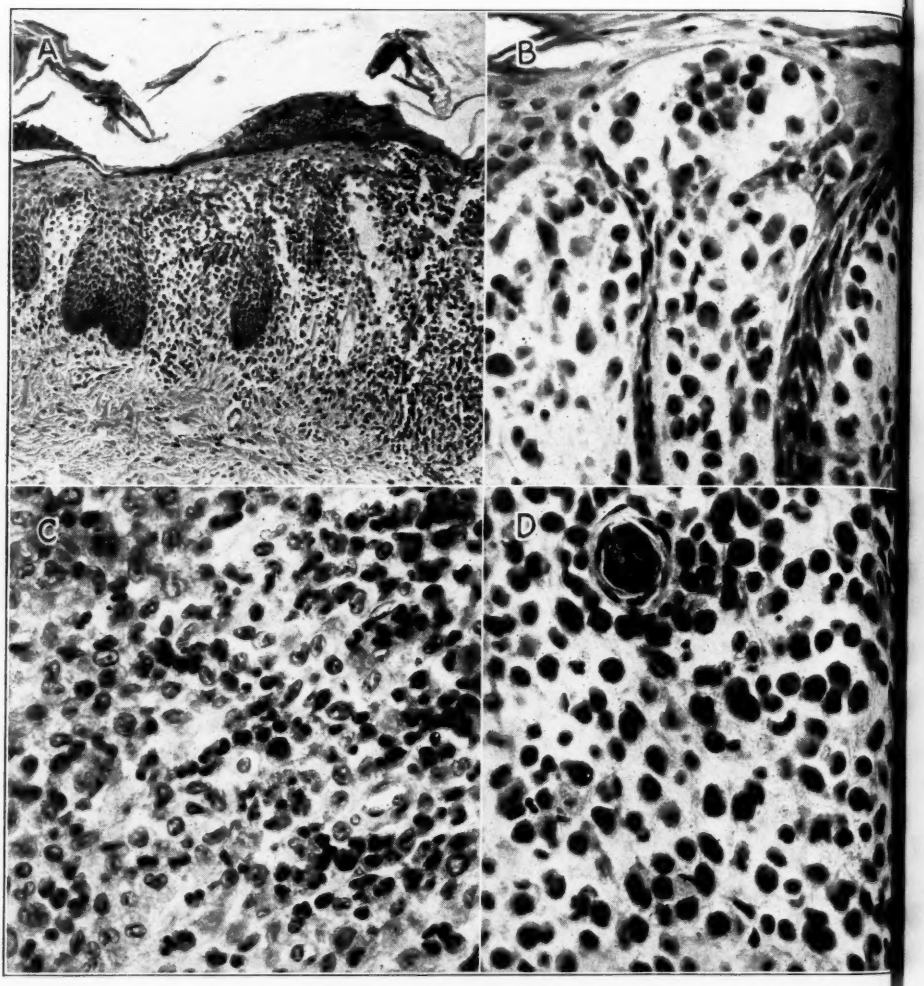

Fig. 2 (case 1).—*A*, skin of chest, low magnification. The upper part of the corium contains an infiltrate composed almost entirely of loosely aggregated histiocytes. The infiltrate has invaded the epidermis in many areas; × 100. *B*, skin of chest, high magnification. The histiocytes of the infiltrate show irregularly shaped nuclei and abundant cytoplasm. In the center the infiltrate has invaded the epidermis; × 400. *C*, granulation tissue removed from the mastoid. The infiltrate consists predominantly of large histiocytes which are densely packed. On the right a large cluster of eosinophils is present; × 400. *D*, granulomatous tumor above the left ear. Large histiocytes are embedded in an edematous stroma. A few scattered eosinophils are present; × 400.

A specimen of granulation tissue removed by curettage from the mastoid during the mastoidectomy on May 7 revealed a densely packed infiltrate of large histiocytes into which large and small clusters of eosinophils were embedded here and there (fig. 2*C*). In addition, eosinophils were sprinkled throughout the histiocytic infiltrate. Lymphocytes were found in small numbers. In some areas of the infiltrate dilated capillaries and extravasated erythrocytes were present. There were a few giant cells which evidently had arisen from the histiocytes of the infiltrate; some of these giant cells were of the foreign body type and others of the Langhans type.

A specimen obtained from the granulomatous tumor on the scalp showed numerous loosely arranged, large histiocytes lying within a decidedly edematous stroma (fig. 2*D*). A few mitotic figures were present within the histiocytes. Eosinophils were scattered among the histiocytes in small numbers. There were numerous dilated capillaries and, here and there, extravasated erythrocytes. In one area a moderate number of lymphocytes and a few plasma cells were intermingled with the histiocytes.

Fig. 3 (case 2).—Two of the four purplish patches are shown. One is located on the left side of the forehead and one in the left zygomatic region.

CASE 2.—*Cutaneous lesions consisting of torpid, asymptomatic, purplish patches on the face.*

A man aged 32, of Irish descent, visited the Dermatologic Clinic of the Massachusetts General Hospital on April 1, 1949 because of four slowly enlarging asymptomatic patches on his forehead and cheeks. The initial lesion had appeared about one year earlier on the forehead and had measured approximately 1 cm. in diameter when first noted by the patient. The three other lesions were of six months' duration or less. The patient had always been of good health and, in the past year, had gained 15 pounds (6.8 Kg.).

On physical examination four lesions were noted on the face. Two plaques measuring 2.5 by 1.5 cm. and 0.7 by 0.7 cm., respectively, were located on the forehead; one plaque, measuring 1.0 by 1.0 cm., was present on the left cheek, and one, measuring 1.5 by 1.0 cm., was present on the right cheek. All were purplish

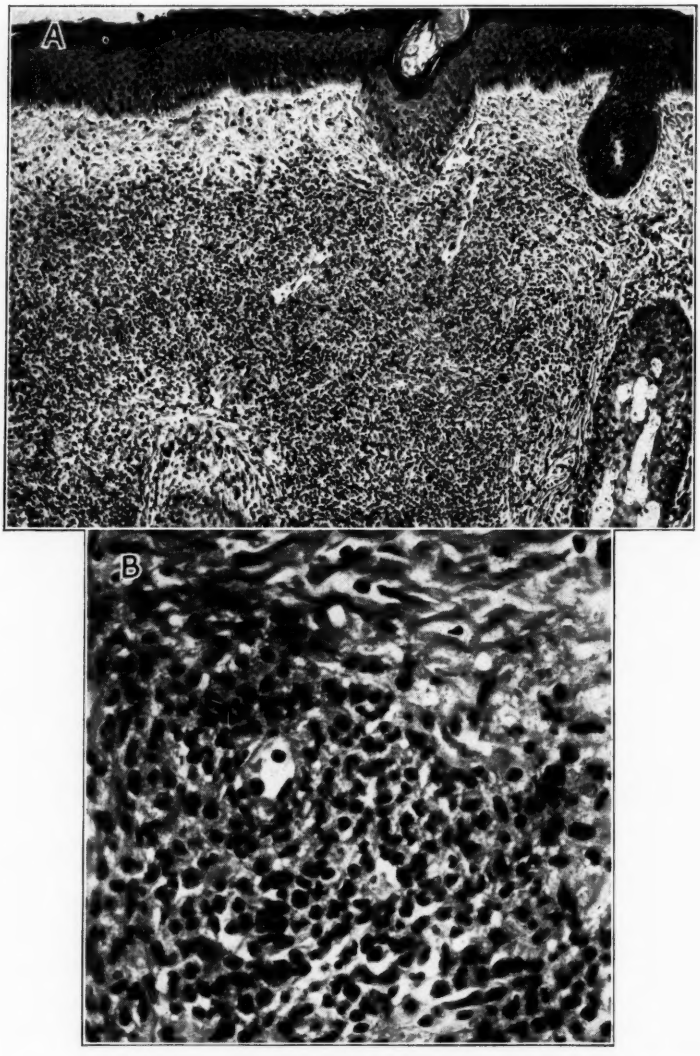

Fig. 4 (case 2).—*A*, lesion on the forehead, low magnification. A dense infiltrate containing many eosinophils is present in the corium. The infiltrate does not invade the epidermis or the sebaceous gland shown on the right but is separated from them by a zone of normal collagen; × 100. *B*, lesion on the forehead, high magnification. The infiltrate consists of intermingled eosinophils, neutrophils and histiocytes. The collagen around the capillary in the center of the photograph is broken up and degenerated; × 400.

tan, slightly elevated and sharply demarcated (fig. 3). Excepting a slight prominence of the follicular openings, the epidermis appeared normal. On palpation the lesions felt soft. The remainder of the physical examination revealed nothing abnormal.

Laboratory Data.—The Hinton test of the blood for syphilis gave negative reactions. Results of urinalysis were normal. The white blood cell count was 11,200. The hemoglobin was 15.4 Gm. per hundred cubic centimeters. A differential count showed 70 per cent neutrophils, 23 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophils. The serum cholesterol measured 188 mg. per hundred cubic centimeters. Roentgenologic examination of the chest revealed no abnormalities.

Histologic Examination.—A specimen obtained from one of the lesions on the forehead revealed an epidermis of normal thickness. The rete pegs, however, were absent. A dense, diffuse infiltrate was present in the upper portion of the corium (fig. 4*A*). Nowhere did the infiltrate invade the epidermis or the pilosebaceous appendages, but it was separated from them by a narrow zone of normal collagen. The infiltrate was polymorphous (fig. 4*B*). It was composed predominantly of polymorphonuclear eosinophils and neutrophils, but histiocytes, lymphocytes and a few plasma cells were also present. The capillaries were dilated, and their endothelial lining was prominent. The infiltrate tended to be densest around the capillaries. Around some of the capillaries the collagen appeared to be broken up and degenerated.

CASE 3.—*Cutaneous lesions consisting of torpid, asymptomatic, purplish patches on the face.*

A man aged 45, of Irish descent, visited the Dermatologic Clinic on June 15, 1949, because of the presence of two purplish brown asymptomatic patches on his left cheek. The larger patch had first been noted ten years previously and had since slowly grown in size. The smaller patch had first appeared one year before. The patient had been known to have arterial hypertension with retinopathy since 1947.

On physical examination the patient appeared well. One plaque measuring 2.0 by 2.5 cm. was present in the right zygomatic region. Another measuring 0.4 by 0.4 cm. was located in front of the right ear lobe (fig. 5). Both lesions were purplish brown, slightly elevated and soft on palpation. Their border was distinct and regular. A few fine telangiectases were present. The pilosebaceous openings were slightly more prominent than usual, but otherwise the epidermis appeared normal.

The retinal veins were tortuous and appeared sclerotic. There was arteriovenous nicking. The heart was slightly enlarged to the left. The blood pressure measured 160 systolic and 122 diastolic. The remainder of the examination revealed no abnormalities.

Laboratory Data.—The reactions to the Hinton test of the blood for syphilis were negative. Observations on urinalyses, a phenolsulfonphthalein excretion test and intravenous pyelography were normal. The white blood cell count was 6,100. The hemoglobin was 16.5 Gm. The differential count revealed polymorphonuclear leukocytes, 74 per cent; lymphocytes, 26 per cent, and eosinophils, none. The serum cholesterol measured 265 mg. per hundred cubic centimeters. Roentgen examination of the chest showed slight tortuosity of the aorta and hypertrophy of the left ventricle. The electrocardiogram showed left ventricular strain consistent with hypertension.

Histologic Examination.—In a specimen removed from the larger plaque the epidermis appeared normal except for some flattening of the rete pegs. The upper part of the corium showed an infiltrate consisting of variously sized, partly confluent

patches which were separated by strands of fibrosis (fig. 6). The infiltrate was separated everywhere from the epidermis and from the pilosebaceous appendages by a narrow zone of normal collagen. The infiltrate was polymorphous, showing

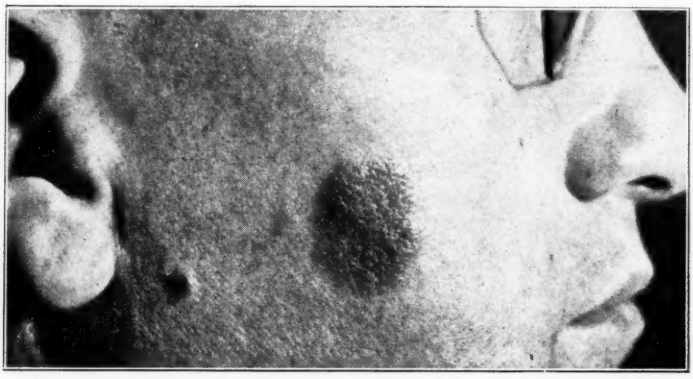

Fig. 5 (case 3).—The two purplish patches located on the right side of the face are shown. The larger patch shows dilatation of the follicular openings.

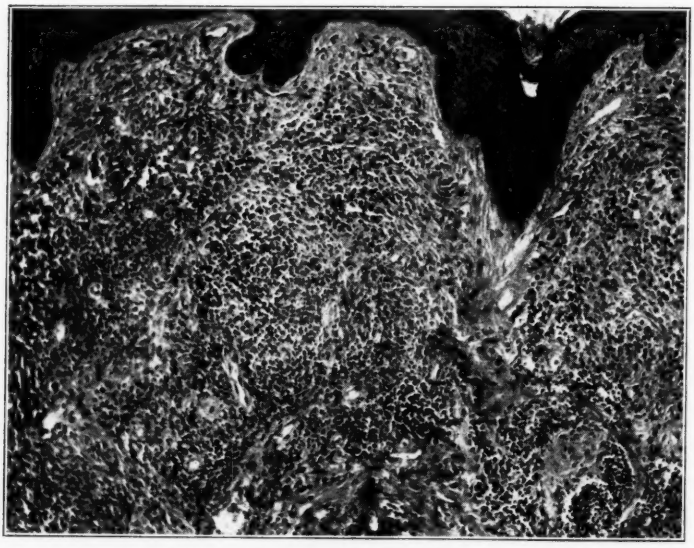

Fig. 6 (case 3).—Lesion in the zygomatic region. The infiltrate is broken up into irregularly shaped patches by strands of collagen. Eosinophils and neutrophils predominate in some areas, and plasma cells in others; × 100.

eosinophils, neutrophils, histiocytes, lymphocytes, plasma cells and fibroblasts. In some areas eosinophils and neutrophils predominated; in others, plasma cells and

lymphocytes. Many capillaries were present in the infiltrate. A few were dilated, but most capillaries were narrow. Some showed disintegration of the collagen in their vicinity; others, especially those located in areas where lymphocytes and plasma cells predominated, were surrounded by fibrosis.

COMMENTS

The first case was that of a small child with lesions in the external ear canal and in the petrous bone which, on histologic examination, were regarded as eosinophilic granuloma of the bone. The cutaneous eruption on the trunk consisted of numerous closely set, brownish, scaling and crusted papules. In addition, a solitary granulomatous tumor was present on the scalp. Since the histologic picture of the cutaneous lesions was the same as that of the osseous lesion, the cutaneous lesions were regarded as manifestations of eosinophilic granuloma.

A review of the literature revealed that, so far, 4 cases have been described in which eosinophilic granuloma of the bone was associated with cutaneous lesions.[2] The cutaneous lesions in these cases were of three types: 1. Small yellowish or brownish keratotic, scaling papules which by coalescence formed a diffuse eruption resembling seborrheic dermatitis were encountered in 3 of the reported cases.[3] 2. Granulomatous, eroded plaques were present in 1 case.[1e] 3. Fluctuant masses were observed in 2 cases [1g,i]; in 1 of these cases [1g] some of the fluctuant masses had broken through the skin, this development resulting in sinus tracts and undermining ulcers. It is of interest that in all 4 cases reported in the literature, as well as in our case, the lesions had their onset in infancy and responded satisfactorily to administration of moderate fractional doses of roentgen rays. Histologic examination of the cutaneous lesions revealed in the 3 previously reported cases in which histologic examination was carried out [4] a picture similar to that observed in our case. Loosely aggregated histiocytes possessing large pale nuclei and abundant acidophilic cytoplasm were present. The number of eosinophils in the 3 cases varied. In 1 case [1e] there were in places a great many eosinophils. In the second case [1g] eosinophils were few and other inflammatory cells were scattered among the sheets of histiocytes. In the third case [11] the histiocytic infiltrate contained a sprinkling of lymphocytes and eosinophils as well as a few mast cells. Lipid was not present in the cutaneous lesions of any of the 3 cases, and it was absent in our case.

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2. (*a*) Curtis and Cawley.[1e] (*b*) McCreary.[1g] (*c*) Pinkus, Copps, Custer and Epstein.[11] (*d*) Kendrick, J. I., and Woodruff, J. B.: Eosinophilic Granuloma: Report of a Case with Both Osseous and Cutaneous Lesions, Cleveland Clin. Quart. **15**:26, 1948.

3. (*a*) Curtis and Cawley.[1e] (*b*) Pinkus, Copps, Custer and Epstein.[11] (*c*) Kendrick and Woodruff.[2d]

4. (*a*) Curtis and Cawley.[1e] (*b*) McCreary.[1g] (*c*) Pinkus, Copps, Custer and Epstein.[11]

The resemblance of the cutaneous lesions from both the clinical and the histologic point of view to those of Letterer-Siwe disease and Hand-Schüller-Christian disease was emphasized by several authors.[4] Such resemblance can be expected since it has been established beyond any doubt that Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma of the bone represent variants of the same disease process.[5] Actually, eosinophilic granuloma of the bone may be regarded as an abortive form of Hand-Schüller-Christian disease.

The second and third cases of this report were of adults with soft, purplish, slowly growing and asymptomatic patches limited to the face. Clinically as well as histologically, these 2 cases were very similar to 6 of the cases reported in the literature as eosinophilic granuloma of the skin [6] and to 1 case recently reported as facial granuloma with eosinophilia [1j]. In all these cases one or several facial lesions were present. In only 1 case were there lesions elsewhere on the skin, namely on the back.[1h] The size of the lesions varied from a few millimeters to 5.5 cm. in diameter. Histologic changes in these 7 cases were similar to those in our 2 cases. The histologic picture may be summarized as follows: A granulomatous infiltrate is located mainly in the upper half of the corium. Quite characteristically, it does not invade the epidermis or the pilosebaceous appendages but is separated from them by a narrow zone of collagen. The pilosebaceous appendages are well preserved. Two stages may be differentiated in the development of the infiltrate, an early "leukocytic" and a late "fibrotic" stage. The two stages may occur together in the same lesion. In the early "leukocytic" stage, eosinophils and polymorphonuclear leukocytes predominate, histiocytes are found in moderate number and, in addition, lymphocytes, a few plasma cells and an occasional mast cell are present. The infiltrate thus has a polymorphous appearance. The capillaries are dilated and surrounded by degenerated collagen. The arrangement of the infiltrate and its composition result in a histologic picture which, like the clinical picture, is different from that of any other disease and, therefore, is diagnostic. In some of the reported cases the histiocytes showed phagocytic activity and contained hemosiderin. Stainable lipids were present within histiocytes in 2 cases.[1d,j] In one of these cases [1d] there was a moderate number of foam cells. In the late fibrotic stage the infiltrate is broken up into variously sized patches by strands of collagen. The number of eosinophils and polymorphonuclear leukocytes is greatly

5. Farber, S.: The Nature of "Solitary or Eosinophilic Granuloma" of Bone, Am. J. Path. **17**:625, 1941. Mallory, T. B.: Medical Progress: Pathology, Diseases of the Bone, New England J. Med. **227**:955, 1942.

6. (*a*) Buley.[1a] (*b*) Lever.[1d] (*c*) Lever, Lane, Downing and Spangler.[1h] (*d*) Wigley, J. E. M.: ? Sarcoid of Boeck; ? Eosinophilic Granuloma, Brit. J. Dermat. **57**:68, 1945.

reduced, and plasma cells, lymphocytes and fibroblasts are numerous. The capillaries tend to have a fibrotic wall.

In the 2 cases reported here the specimen removed for biopsy in the first case was in the early "leukocytic" stage, while that taken in the second case showed an intermediate phase between the "leukocytic" and "fibrotic" stage.

The disease does not seem to be associated with any internal lesions. It apparently represents a disease *sui generis* the etiology of which is so far unknown. The disorder is not a rare one since 6 cases have been observed in Boston within a few years.[1d,h] Inasmuch as the disease is not rare and possesses a distinct clinical and histologic picture it is surprising that it was never described in the literature prior to 1945. It is perhaps possible that 1 of the patients whose case was reported by Hutchinson,[7] under the diagnosis of purple patches on the skin, had the disease under discussion, but since no histologic examination was carried out a definite decision cannot be made.

DIFFERENTIATION OF THE TWO TYPES OF EOSINOPHILIC GRANULOMA OF THE SKIN

The two types of eosinophilic granuloma just described were at first regarded as one and the same disease.[8] One of the reasons for this opinion was that in Lever's first case [1d] the histologic sections showed foam cells which suggested a lipidization process like that occurring in eosinophilic granuloma of the bone and in Hand-Schüller-Christian disease. Recently, however, the clinical and histologic dissimilarity of the two types of eosinophilic granuloma was recognized by Pinkus, Copps, Custer and Epstein,[11] by Cobane, Straith and Pinkus [1j] and by Lever.[9] Pinkus and co-workers [11] rightly pointed out that lipidization is a nonspecific process which is not peculiar to any group of diseases but may occur in a variety of diseases.

Clinically the cutaneous lesions of eosinophilic granuloma of the bone occur in young children, are associated with osseous lesions and may occur anywhere on the skin except that they seem to spare the face. The lesions consist of yellowish scaling papules, of yellowish firm plaques which may become eroded or of irregular undermining ulcers. The lesions are radiosensitive. On the other hand, in the eosinophilic granuloma characterized by purplish patches of the face the lesions occur in adults, are exclusively or predominantly located on the face, are covered by a normal-appearing epidermis, do not ulcerate and are radioresistant.

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7. Hutchinson, J.: Two Additional Cases of Purple Patches on the Skin: History of Gout in Both, Arch. Surg. **1**:372, 1890 (case 2).

8. Lever.[1d] Wigley.[6d]

9. Lever, W. F.: Histopathology of the Skin, Philadelphia, J. B. Lippincott Company, 1949, p. 223.

The histologic picture too differs in the two diseases, except that both show many histiocytes and usually also many eosinophils in the infiltrate. In the cutaneous lesions of eosinophilic granuloma of the bone the infiltrate is composed almost entirely of large histiocytes. The amount of eosinophils varies. They may be few. When present in large numbers they tend to lie in patches. The infiltrate tends to invade and to destroy the epidermis. On the other hand, in eosinophilic granuloma of the skin characterized by purplish patches on the face one observes a polymorphous infiltrate with vascular changes. The eosinophils are diffusely scattered through the infiltrate. The epidermis is never invaded by the infiltrate.

Little needs to be said about the third, heterogeneous group of cases of eosinophilic granuloma of the skin. Preponderance of eosinophils in a granulomatous infiltrate may occur in many different diseases. To make the preponderance of such a ubiquitous cell as the eosinophil the criterion of a diagnosis is therefore inadvisable. A perusal of the cases collected in Weidman's paper on eosinophilic granulomas of the skin [1b] and of those reported by Collins [10] and Thoroczkay [11] under this diagnosis will convince one of the inadvisability of such an undertaking. Weidman pointed out that the actual diagnosis in cases reported as eosinophilic granuloma of the skin includes lymphoma, tuberculosis and fungous infections.

Since no relation seems to exist between the two disease entities which are at present called eosinophilic granuloma we are inclined to agree with Cobane, Straith and Pinkus [1j] that an adjustment in the nomenclature of these two diseases is desirable. Inasmuch as the term eosinophilic granuloma has been in use longer for the disease with osseous lesions than for the disease characterized by facial lesions it is appropriate that the term be retained for the former. Cobane, Straith and Pinkus [1j] suggested the term facial granuloma with eosinophilia as a designation for the disease with facial lesions. This purely descriptive term may well be used until more is known about the pathogenesis of this disease.

SUMMARY

At present two entirely different cutaneous diseases are known under the same diagnostic term, eosinophilic granuloma.

One disease has osseous lesions in conjunction with the cutaneous lesions and represents an abortive form of Hand-Schüller-Christian disease. The other disease has only cutaneous lesions, predominantly on the face, and represents a disorder *sui generis* of unknown etiology.

On the basis of 3 cases the differences in the clinical and histologic picture of the two diseases are discussed.

10. Collins, C. L.: Eosinophilic Granuloma, Proc. Roy. Soc. Med. **39**:682, 1946.

11. Thoroczkay, N.: Case of Eosinophilic Granuloma, Rev. Dermat. & Venereol. **9**:267, 1947; abstracted Excerpta Med. (sect. 13) **2**:211, 1948.

PRIMARY CUTANEOUS CRYPTOCOCCOSIS

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GENERALIZED systemic and cerebrospinal cryptococcosis (torulosis) are accepted clinical entities. The extensive monograph by Stoddard and Cutler [1] published in 1916 firmly established their identity. The cutaneous manifestations are apparently recognized infrequently. The literature contains few authentic examples.[2] Primary cutaneous cryptococcal infection in which the skin lesions are the sole manifestation of the disease, without a preceding generalized or cerebrospinal involvement, seems to be rarer still. In any form, however, the condition is often associated with other disease entities. This report will present a case of cutaneous cryptococcosis which apparently represents the *sui generis* form of the disease, associated with sarcoidosis.

REPORT OF A CASE

The patient was a white divorced woman aged 29, a lifetime resident of New Orleans. She stated that she had been "anemic" and afflicted with "enlarged glands" since childhood. She had measles, mumps, chickenpox and scarlet fever in early life. Except for repeated attacks of tonsillitis and infection of the upper respiratory tract there had been no serious illness prior to 1942. In that year, while residing briefly in Cleveland, she had become pregnant and her physician had noted "enlarged glands" of the neck and upper and lower extremities. Histologic study of an excised inguinal lymph gland led to a diagnosis of Boeck's sarcoid. After the birth of her baby, she had acquired extensive condylomata acuminata involving the anogenital region, which were treated with roentgen rays

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From the Louisiana State University Service, Department of Dermatology and Syphilology, Charity Hospital of Louisiana, New Orleans, under the direction of Dr. James K. Howles and the Department of Microbiology, Louisiana State University School of Medicine.

1. Stoddard, J. L., and Cutler, E. C.: Torula Infection in Man, Monograph 6, Rockefeller Institute for Medical Research, 1916.

2. (*a*) McGehee, J. L., and Michelson, I. D.: Torula Infection in Man, Surg., Gynec. & Obst. **24**:803, 1926. (*b*) Urbach, E., and Zach. F.: Generalized Torulosis, Arch. f. Dermat. u. Syph. **162**:401, 1930. (*c*) Weidman, F. D.: Cutaneous Torulosis, South. M. J. **26**:851, 1933. (*d*) Wile, U. J.: Cutaneous Torulosis, Arch. Dermat. & Syph. **31**:58 (Jan.) 1935. (*e*) Mook, W. H., and Moore, M.: Cutaneous Torulosis, ibid. **33**:951 (June) 1936. (*f*) Torrey, F. A.: Cutaneous Torulosis in a Patient with Hodgkin's Disease, ibid. **55**:738 (May) 1947. (*g*) Versé, M.: Ueber einen Fall von generalisierter Blastomykose beim Menschen, Verhandl. d. deutsch. path. Gesellsch. **17**:275, 1914.

at weekly intervals over a period of several months. The lesions failed to regress, and application of ointment of resin of podophyllum was then tried. This treatment resulted in a severe burn followed by a slough of much of the vulva. The patient had one child living and well, and the family history was irrelevant.

The patient had been under continuous observation and treatment at the Charity Hospital of Louisiana at New Orleans since July 2, 1945. Successive complaints brought her at one time or another to the attention of the medical, surgical, gynecologic and dermatologic services. During the period between July 1945 and December 1947 the following diagnoses were entered on her clinical record: sarcoidosis without cutaneous manifestations, condylomata acuminata, bilateral renal calculi and bilateral venous thrombosis of the lower extremities. During 1947 she underwent a vulvectomy, nephrolithotomy (right), vaginal ureterotomy and several minor surgical procedures.

Dermatologic Examination.—The patient was first seen by us on Aug. 14, 1947, presenting a lesion on the left side of the face of three months' duration. The onset had been in the form of several small discrete "blisters," draining a sticky secretion, which, through enlargement and coalescence, had produced the present "growth" in three to four weeks, with no subsequent change in size or appearance (fig. 1).

Examination revealed a roughly triangular lesion, 2 by 1 by 7 cm., located at the junction of the left cheek with the nose about midway between the left inner canthus and left ala nasi. It was a slightly but distinctly elevated soft, dusky brown granuloma with a depressed center and covered with a dark crust. A small amount of serosanguinous exudate appeared on removal of the crust. There was no surrounding erythema and no induration. The lesion was painless. A biopsy specimen was taken; the tissue was extremely soft, almost gelatinous. Microscopic and cultural studies revealed the presence of Cryptococcus neoformans.

Course of Illness.—After promin® (sodium p,p′-diaminodiphenylsulfone-N,N′-didextrose sulfonate) therapy in the medical service, consisting of the administration of 4 Gm. intravenously twice daily for a total of 124 Gm. (treatment was then discontinued because of unfavorable reactions), the patient was transferred to the dermatologic service on Dec. 17, 1947, four months after the biopsy specimen was obtained. The original lesion on the face had regressed to a small cicatricial plaque. A new lesion, over the left zygoma, consisting of a roughly circular salmon-colored scaly patch had developed within the week prior to this admission. From this area cryptococci were cultured and identified.

Physical examination showed the patient to be in moderately good health. There was generalized superficial lymphadenopathy consisting of firm, discrete, freely movable nodes. The liver and spleen were not palpable. The labia majora and minora had been removed surgically. No abnormal masses were found on pelvic examination. The neurosurgical service reported that the results of a neurologic examination were essentially normal. The patient remained afebrile during her stay on the dermatologic service.

Laboratory Data.—Studies of the blood yielded the following results: The red cells numbered 2,820,000, and the white cells, 3,200. The differential count showed 74 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes, 7 per cent monocytes and 2 per cent eosinophils. The hemoglobin determination was 9.8 Gm. The sedimentation rate (Wintrobe method) was 40 mm. per hour uncorrected and 62 mm. per hour corrected. The blood platelet count was 120,000. The mean corpuscular volume was 106 cc., and the mean corpuscular hemoglobin, 34 micrograms. The blood serum gave negative Kolmer, Wassermann and Kahn reactions on two occasions. The blood chemistry figures were as follows: urea nitrogen,

22.6 mg.; cholesterol, 180 mg.; calcium, 11.2 mg.; inorganic phosphates, 3.8 mg.; alkaline phosphatase, 2.0 Bodansky units per hundred cubic centimeters, and bromide level, 5.8 per cent. There was a reversal of the albumin-globulin ratio. The urine showed no abnormalities except a variable number of white blood cells per high power field. The sputum revealed no fungi or acid-fast bacilli on several

Fig. 1.—Lesion of cutaneous cryptococcosis.

examinations. The chemistry of the spinal fluid was normal, and the fluid yielded no evidence of fungi or yeasts as determined by direct smear, india ink preparation or culture on repeated search. Reactions to the tuberculin test with graded dilutions of old tuberculin were completely negative. Roentgenologic investigation of the chest and bones of the hands revealed no significant abnormalities.

Histologic Studies.—Sections stained with hematoxylin and eosin revealed moderate acanthosis of the rete mucosum. The deeper layers of the cutis were

heavily infiltrated with lymphocytes, proliferating fibroblasts and a few plasma cells. Virtually no polymorphonuclear leukocytes were present. Throughout the infiltrate numerous giant cells of the foreign body type were irregularly scattered. These cells contained pink-staining, highly refractile yeastlike organisms

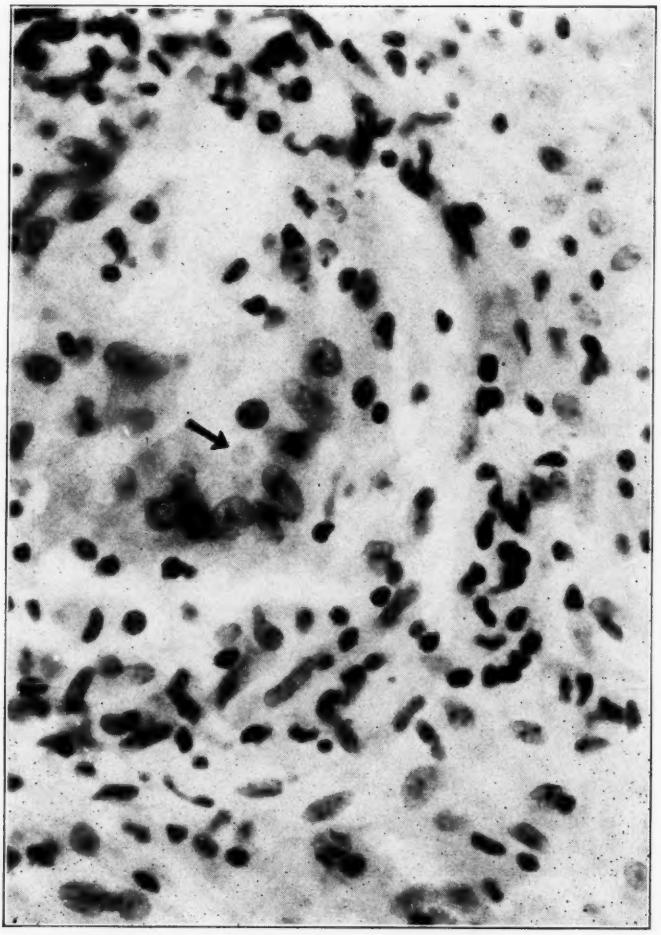

Fig. 2.—High power magnification of section showing encapsulated cryptococcic organism within lower portion of large giant cell.

which had a conspicuous double contour (fig. 2). The only other notable feature was a thickening of the arteriolar walls with no distinct perivascular infiltrate.

A biopsy specimen obtained from an enlarged cervical node was reported as showing a picture compatible with sarcoidosis. Sections from an inguinal node

which had been previously examined on the medical service were reviewed and likewise found to present changes consistent with sarcoidosis. This impression was confirmed by Dr. F. D. Weidman of Philadelphia. No yeastlike organisms could be found in stained sections from the aforementioned cervical node. Cultures of material from this node did not yield bacteria or fungi. Finally, a review of the

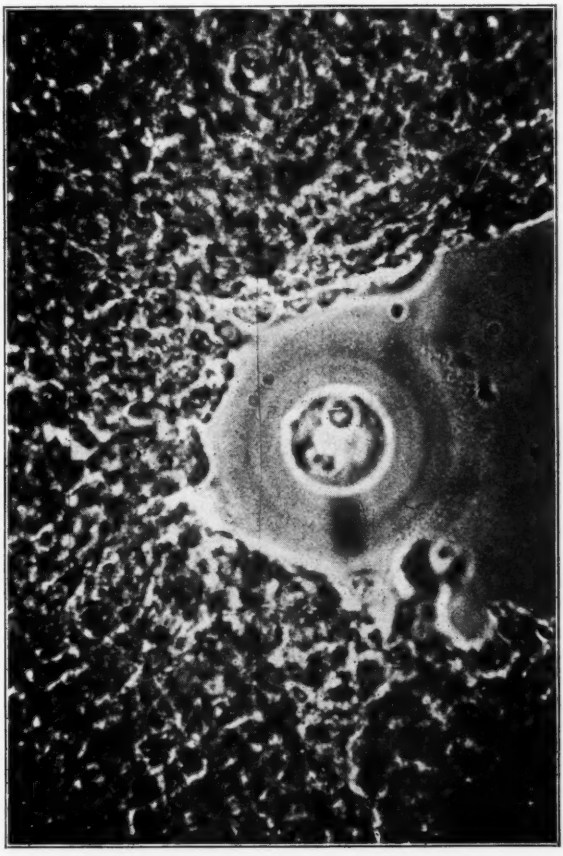

Fig. 3.—Photograph (× 750) of organism observed in direct examination of fresh tissue.

sections from the vulva confirmed the original diagnosis of condyloma acuminatum and excluded the presence of yeastlike organisms.

Mycologic Studies.—Direct microscopic examination of a fresh specimen of tissue from the cutaneous lesion revealed encapsulated yeastlike organisms which were tentatively identified as cryptococci (fig. 3). The tissue was ground under aseptic conditions, and 100 units of penicillin and 50 units of streptomycin were

added. Sabouraud's medium and blood agar plates inoculated with this material were incubated, and large gelatinous colonies appeared in four days (fig. 4). India ink preparations revealed yeastlike cells surrounded by wide capsular zones (fig. 5).

Animal Inoculation.—Twelve white mice were inoculated intraperitoneally with 0.5 cc. each of a suspension of these cultures. One mouse was dead on the tenth day; 5 were dead on the twelfth, 3 on the fifteenth, 2 on the eighteenth and the remaining one on the twenty-first day after inoculation. Encapsulated yeastlike organisms were demonstrable in preparations of the mesentery, liver, spleen, lungs

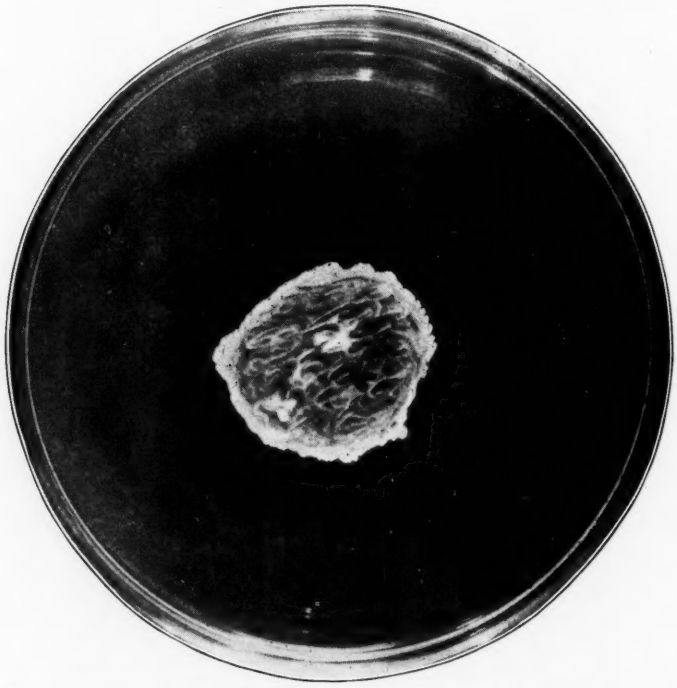

Fig. 4.—Culture on Sabouraud's glucose agar at the end of four days, at room temperature. A typical gelatinous colony is demonstrated.

and brain of each animal. Subcultures on Sabouraud's medium and blood agar (of material secured from the various sites of the inoculated animals) incubated at room temperature all grew encapsulated yeastlike organisms in pure culture.

These procedures appeared to establish unequivocally the identity of the microorganisms recovered from the biopsy specimen as C. neoformans.

Treatment was begun with the administration of 1 Gm. of sulfadiazine four times daily but had to be discontinued after three days because of severe nausea and vomiting. Under treatment with supportive measures, including frequent small transfusions, the administration of vitamins, iron preparations and crude liver extract, striking improvement took place. The patient was discharged from

the hospital approximately six weeks after the date of admission and was referred to the dermatologic clinic but disappeared from observation.

Subsequent Course.—In April 1949 the patient was discovered by chance on the urologic service at Charity Hospital. More than a year had elapsed since our last contact with her. Meanwhile she had remarried. She had not returned to the dermatological clinic because her skin lesions had healed. She appeared debilitated and chronically ill. There was an open, draining sinus in the region of the right kidney. Cultures from the sinus material revealed Pseudomonas aeruginosa. The urologic diagnosis was right perirenal abscess and nephrocalcinosis with early uremia.

The facial sites of the original lesions of cutaneous cryptococcosis were marked by inconspicuous scars. The generalized lymphadenopathy was still present.

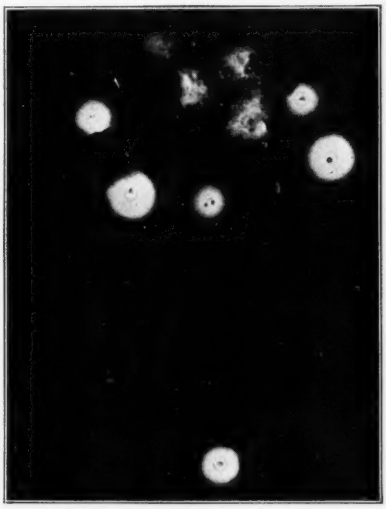

Fig. 5.—India ink preparation of material grown on Sabouraud's glucose agar, showing wide capsular zones surrounding organisms.

Further physical or laboratory investigations were not possible at the time because of the patient's uncooperative attitude and the severity of her illness. At the time of writing, May 1949, she was still a patient on the urologic service.

COMMENT

When the diagnosis of cutaneous cryptococcosis had been satisfactorily established, the possibility of a concomitant systemic infection was recognized, but no evidence of this was found. In most of the reported cases of this disease cerebrospinal involvement which proved to be lethal developed. Whether this will be the final outcome in our patient, if she survives renal or other intercurrent complications, or whether she will acquire permanent immunity to the cryptococcal infection is for the

future to determine. An interesting sidelight on this case was the observation of associated sarcoidosis, although our studies established it only for the lymph glands.

Cutaneous cryptococcosis has been experimentally produced in the monkey by Weidman.[2c] The pathogenesis of the experimental disease closely duplicates what has been observed in the case described in this report. The question then arises: Can primary cryptococcal infection of the skin produce a dermatologic lesion which presents a fairly typical morphologic picture? In our patient the granulomatous appearance, the gelatinous consistency and the absence of surrounding erythema, induration or suppuration were the characteristic features.

SUMMARY

A case of primary cutaneous cryptococcosis is reported.

The clinical course of the disease and the gross and microscopic features of the lesions are described.

C. neoformans was identified in culture.

Experimental animals were successfully infected.

424 Medical Arts Building.

VERRUCOUS AND PAPILLOMATOUS TYPES OF SARCOID

Report of a Case

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VERRUCOUS and papillomatous types of sarcoid are uncommon. In view of their rarity it seemed appropriate to report a case of sarcoidosis which showed the verrucous and papillomatous forms of this disease in addition to the common nodular type of eruption and sarcoid tumors.

REPORT OF CASE

I. W., a Negro aged 25, entered the clinic complaining of a cutaneous eruption and swelling of the fingers. The eruption had been first noticed eight years previously, originating as two large warty lesions which had appeared simultaneously on the right knee. Subsequently two additional small verrucous nodules developed on the right knee and another on the right buttock. These hyperkeratotic lesions were mildly hyperpigmented and roughly round and oval. After several months the fingers began to enlarge rapidly. The swollen fingers were painless, firm and flesh colored, and their nails were dystrophic. A few years later both fifth fingers were amputated because of superimposed traumatic ulcerations. Two years after the onset of the initial eruption two small papillomatous lesions developed in symmetric fashion on the back of the neck; they were flesh colored and pedunculated, and their surfaces were flat and rough. Shortly thereafter tumor-like lesions appeared on the posterior aspect of each arm. These tumefactions were firm, reddish and slightly scaly; three small, closely aggregated ones were present on the left arm, and a single large tumor was noted on the right. About five years after the cutaneous lesions were first noted and shortly after the patient's recovery from chickenpox, the eruption became widespread. The face was particularly affected, but many lesions were also present on the buttocks; smaller numbers developed on the lower extremities and a few on the buccal mucosa. The generalized eruption consisted of pinhead-sized to match head-sized pinkish, reddish and brownish nodules which had a decided tendency to group and coalesce to form small, slightly scaly patches. The lymph nodes of the posterior cervical and inguinal chains were moderately enlarged, asymptomatic, discrete and freely movable.

Laboratory Data.—An intracutaneous injection of 0.01 cc. of old tuberculin in dilution of 1:100 produced a weakly positive local reaction. A Kahn test of the

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blood gave a negative reaction. A hemogram showed 4,400 leukocytes, with 46 per cent lymphocytes and 10 per cent monocytes. The blood serum albumin was diminished (to 3.92 Gm. per hundred cubic centimeters), and the globulin showed an increase (to 3.21 Gm. per hundred cubic centimeters).

Roentgenograms of the chest and hands showed pictures which were consistent with those of pulmonary and osseous sarcoid.

Histologic examination of a verrucous lesion from the knee showed a typical sarcoid type of infiltrate which was limited to the upper half of the cutis. A limited

Fig. 1.—Four verrucous lesions of sarcoid were present on the right knee.

degree of papillomatosis was present. The prickle cell and granular cell layers of the epidermis were decidedy irregular, and the stratum corneum was immensely thickened; the latter contained small nodules and thin layers of parakeratotic cells. The histologic characteristics in a section of the verrucous lesion from the buttock were similar to those observed in the preceding section except that the tuberculoid infiltrate was limited to the upper fourth of the cutis and papillomatosis was more widespread but the hyperkeratosis was decidedly less.

The papillomatous sarcoid lesion showed an irregular papillary hyperplasia and a tuberculoid infiltrate which was limited to the upper fourth of the cutis. The prickle cell layer of the epidermis was irregularly acanthotic, and the stratum

corneum showed slight to moderate degrees of hyperkeratosis. The most interesting features noted were the thorough admixture of the lymphocytic and epithelioid cell infiltrates and the presence of a keloid within the upper half of the cutis.

The histologic features of Boeck's sarcoid were observed both in a cutaneous nodule and in the tumor from the right arm.

Fig. 2.—A roentgenogram of the hand showed sarcoid involvement of the phalangeal and metacarpal bones.

SUMMARY

A case of sarcoidosis is reported. The cutaneous eruption consisted of nodules and tumors and of verrucous and papillomatous types of lesions. The verrucous eruption was asymmetric.

Histologically, the tuberculoid structures in the verrucous lesions were typical of sarcoid. In one lesion the cellular infiltrates were confined to the upper half of the cutis while in the other they were contained within the upper fourth of this layer. Papillomatosis was observed in both sections.

Fig. 3.—Low power photomicrograph of the papillomatous sarcoid lesion. The large epithelioid tubercle in the subpapillary region is almost obscured by the invading lymphocytic infiltrate; hematoxylin and eosin.

There were two unusual histologic features present in the section of papillomatous sarcoid, namely, thorough admixture of the lymphocytic and epithelioid cell infiltrates and the presence of a keloid within the upper half of the cutis.

160 Riverside Drive (24).

GRANULAR CELL MYOBLASTOMA

Report of a Case Simulating Granuloma Inguinale

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IN 1926 Abrikossoff [1] first described a peculiar tumor which he later concluded was derived from primitive myoblasts and to which he gave the name of "myoblastoma." In 1945 Crane and Tremblay [2] were able to gather 162 cases, including 5 of their own. A review of the literature through September 1949 [3] disclosed an additional 58 cases which with the addition of our own bring the total to 221. Since 20.4 per cent of myoblastomas are of the skin and subcutis, involvement of these areas being second in frequency to involvement of the tongue (37.6

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1. Abrikossoff, A. I.: Ueber Myome ausgehend von der quergestreiften willkürlichen Muskulatur, Virchows Arch. f. path. Anat. **260**:215, 1926.

2. Crane, A. R., and Tremblay, R. G.: Myoblastoma, Am. J. Path. **21**:357 (March) 1945.

3. (*a*) Powell, E. B.: Granular Cell Myoblastoma, Arch. Path. **42**:517 (Nov.) 1946. (*b*) Simon, M. A.: Granular Cell Myoblastoma, Am. J. Clin. Path. **17**:302 (April) 1947. (*c*) Bloom, D., and Ginzler, A. M.: Myoblastoma, Arch. Dermat. & Syph. **56**:648 (Nov.) 1947. (*d*) Cipollaro, A. C., and Einhorn, M. B.: Granular Cell Myoblastoma, ibid. **56**:812 (Dec.) 1947. (*e*) Stout, A. P.: Granular Cell Myoblastoma of the Breast, J. Missouri M. A. **44**:342 (May) 1947. (*f*) Printz, D. R.; Cole, H. N., and Driver, J. R.: Myoblastoma, Arch. Dermat. & Syph. **55**:297 (Feb.) 1947. (*g*) Ackerman, L. V., and Phelps, C. R.: Malignant Granular Cell Myoblastoma of the Gluteal Region, Surgery **20**:511 (Oct.) 1946. (*h*) Kerr, D. A.: Myoblastic Myoma, Oral Surg., Oral Med. & Oral. Path. **2**:41 (Jan.) 1949. (*i*) Bernier, J. L., and Thompson, H. L.: Myoblastoma, Dent. Research **25**:253 (Aug.) 1946. (*j*) Khanoekar, V. R.: Granular Cell Myoblastoma, Am. J. Path. **23**:721 (Sept.) 1947. (*k*) Haagensen, C. D., and Stout, A. P.: Granular Cell Myoblastoma of the Mammary Gland, Ann. Surg. **124**:218 (Aug.) 1946. (*l*) Kraus, A. R.; Melnick, P. J., and Weinberg, J. A.: Myoblastoma of the Bronchus, J. Thoracic Surg. **17**:382 (June) 1948.

per cent),[3a] it is apparent that approximately 50 per cent of the reported cases are of dermatologic interest. Despite this statistical importance, the articles by Tuta and Schmidt,[4] Bloom and Ginzler [3c] and Cipollaro and Einhorn [3d] and the case presentations by Ebert and Slepyan [5] and by Printz [3f] are the only references to this subject in dermatologic literature. We therefore believe that a brief review of the subject and report of a case of unusual type should be recorded.

CLINICAL FEATURES

Myoblastoma usually occurs as a small, firm, nontender nodule, 1 to 2 cm. in diameter, although occasionally it may be larger. The surface is usually intact but may be ulcerated. Most commonly a single, distinct, rounded mass is present, but lobulated, pedunculated, polypoid and sessile tumors have been reported. These have often been mistaken for fibromas or xanthomas.

As previously mentioned, the tongue is most commonly involved, with the skin, alveolar processes, respiratory tract, breast, ear and lip being affected in decreasing order of frequency.

Although the tumors have occurred in all age groups, the greatest incidence has been in the third, fourth and fifth decades. There is no sex predilection.

The course is benign. The lesions are usually slow growing, and local excision suffices in most cases. However, recurrence locally has been reported by Horn and Stout,[6] and the appearance of metastases was observed in the cases described by Geschickter [7] and by Bloom and Ginzler.[3c] Frankly malignant tumors have been reported by von Meyenburg,[8] Morpurgo,[9] Ravich, Stout and Ravich,[10] Powell [3a] and Ackerman and Phelps.[3g] It was suggested by Ravich, Stout and Ravich [10] that this malignant form of myoblastoma actually represents a polymorphous sarcoma and that the term "granular cell myoblastoma" should be reserved for the benign type.

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4. Tuta, J. A., and Schmidt, F. R.: So-Called Myoblastoma, Arch. Dermat. & Syph. **46**:225 (Aug.) 1942.

5. Ebert, M. H., and Slepyan, A. H.: So-Called Myoblastoma, Arch. Dermat. & Syph. **48**:348 (Aug.) 1943.

6. Horn, R. C., Jr., and Stout, A. P.: Granular Cell Myoblastoma, Surg., Gynec. & Obst. **76**:315 (March) 1943.

7. Geschickter, C. F.: Tumors of Muscle, Am. J. Cancer **22**:378 (Oct.) 1934.

8. von Meyenburg, H. Die quergestreifte Muskulatur, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen anatomie und Histologie, Berlin, Julius Springer, 1929, vol. 9, pt. 1, p. 468.

9. Morpurgo, B.: Myoblastomi, Arch. per le sc. med. **59**:229 (Feb.) 1935.

10. Ravich, A.; Stout, A. P., and Ravich, R. A.: Malignant Granular Cell Myoblastoma Involving the Urinary Bladder, Ann. Surg. **121**:361 (March) 1945.

MICROSCOPIC FEATURES

The tumors are composed predominantly of large polyhedral cells, the majority being irregularly rounded. The cells occur in small clusters and in large groups, distributed widely throughout the corium and extending from the papillary layer to the subcutis. The distinctive feature of the cell is the presence of abundant acidophilic granular cytoplasm. Some investigators emphasized that the cytoplasm is vacuolated, while others just as strongly denied this. However, all special stains for lipid have failed to reveal it. In rare cases longitudinal and cross striations have been demonstrated. The nuclei are small, round to oval, centrally located and vesicular; pyknotic forms may be numerous, and mitoses are usually absent.

A significant finding in many tumors is decided proliferation of the epidermis. This pseudoepithliomatous hyperplasia has frequently been misinterpreted and a diagnosis made of squamous cell carcinoma.

HISTOGENESIS OF MYOBLASTOMA

There has been considerable controversy concerning the origin of these tumors. Abrikossoff [1] in his original report described them as arising from striated muscle in the reparative processes resulting from trauma or inflammation. However, in view of Klinge's [11] report of occurrence of myoblastoma in the skin, some other explanation was forthcoming to explain development of this tumor in a site devoid of skeletal muscle. It was suggested by Klinge,[11] and earlier by Pendl [12] and Rütz,[13] that these tumors might originate from primitive myoblasts. Evidence to support this hypothesis was found in the similarity of the tumor cells and immature skeletal muscle fibers.[14] The occurrence of the primitive myoblast in the skin was explained in line with Cohnheim's tumor theory as the result of incomplete separation of the myotome into the corium and skeletal muscle, with the primordial muscle cells being abnormally placed in the cutis.

This concept has not been universally accepted, objection having been raised notably by Gray and Gruenfeld.[15] They suggested that the tumors arising in the tongue have a different histogenesis than have those arising in the skin. They maintained, as did Abrikossoff in his

11. Klinge, F.: Ueber die sogenannten unreifen, nicht quergestreiften Myoblastenmyome, Verhandl. d. deutsch. path. gesellsch. **23**:376, 1928.

12. Pendl, F., cited by Crane and Tremblay.[2]

13. Rütz, A., cited by Crane and Tremblay.[2]

14. Godlewski, E.: Die Entwicklung des Skelet- und Herzmuskelgewebes der Saügethiere, Arch. f. mikr. Anat. **60**:111, 1902.

15. Gray, S. H., and Gruenfeld, G. E.: Myoblastoma, Am. J. Cancer **30**:699 (Aug.) 1937.

original report, that the tumor cells of the former arise, not from misplaced embryonal cells, but rather "in consequence of reparative regenerative tissue reactions, possibly following some mild trauma of the muscle fibers." This belief was based on their observation of a change of mature muscle fibers to the characteristic tumor cells as the result of necrobiosis. They further maintained that there is no basis for the belief that cutaneous myoblastoma arises from primitive muscle cells. They cited the studies by Zechel, Franz and Marcus, who made no mention of granular polyhedral cells in normal myogenesis. Since the dysontogenetic theory is based on the similarity of the tumor cell and a granular cell which appears during the maturation of the primitive muscle cell, they held this theory untenable.

At present the exact histogenesis of myoblastoma is not clearly defined. However, most investigators, including Klemperer,[16] expressed the belief that the tumors arise from misplaced primitive myoblasts, in accordance with the dysontogenetic theory of Klinge.[11]

REPORT OF A CASE

D. C., a 25 year old Negro woman, was seen at Bellevue Hospital in January 1949 complaining of a lesion on her thigh. This had started as a "knot" about one and one-half years before, gradually enlarging and then ulcerating four months prior to her visit to the hospital. The lesion was asymptomatic except for slight pain following friction. The patient's past history was noncontributory except for the fact that from June 27 to July 5, 1947, she had received 4,800,000 units of penicillin as treatment for secondary syphilis. She denied loss of weight, weakness and cough and had no complaints other than those concerning the lesion of the thigh.

Examination revealed a well developed, well nourished woman who was completely normal except for a lesion in the right inguinocrural groove, adjacent to the lower pole of the labium majus (fig. 1). This measured 1.8 by 4.5 cm. and consisted of an ulcer with a truncated, granulomatous base and an elevated, whitish, cordlike border. The surrounding tissues were indurated, and the mass, which was sharply demarcated, could be felt extending fairly deep. Cytologic studies of the blood and urinalysis showed no abnormalities. The serologic tests for syphilis gave negative reactions.

The clinical appearance was suggestive of granuloma inguinale, but numerous attempts to demonstrate Donovan bodies were unsuccessful. At the suggestion of Dr. Simeon E. Landy a piece of tissue was removed for histologic study. The tumor was subsequently excised widely and deeply. The patient was last seen three months later, at which time there was no evidence of recurrence.

The microscopic sections were studied by Dr. W. C. von Glahn (director) and his associates of the Department of Pathology, Bellevue Hospital, who agreed that they were typical of myoblastoma. The lesion at one edge showed pronounced

16. Klemperer, P.: Myoblastoma of the Striated Muscle, Am. J. Cancer **20**:324 (Feb.) 1934.

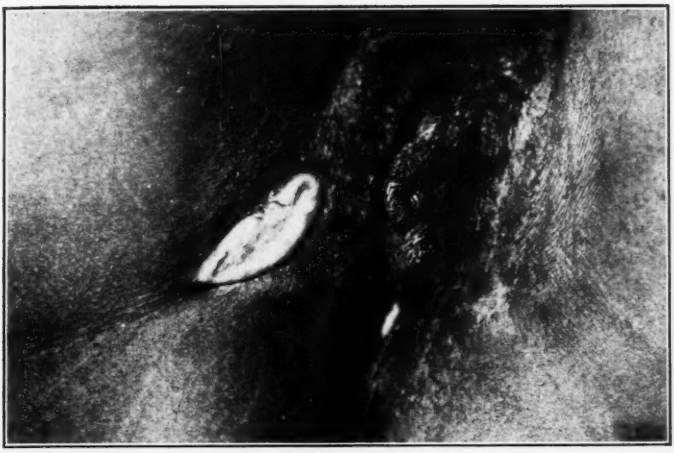

Fig. 1.—Ulcerative lesion of the perineum showing the cordlike border and granulomatous base.

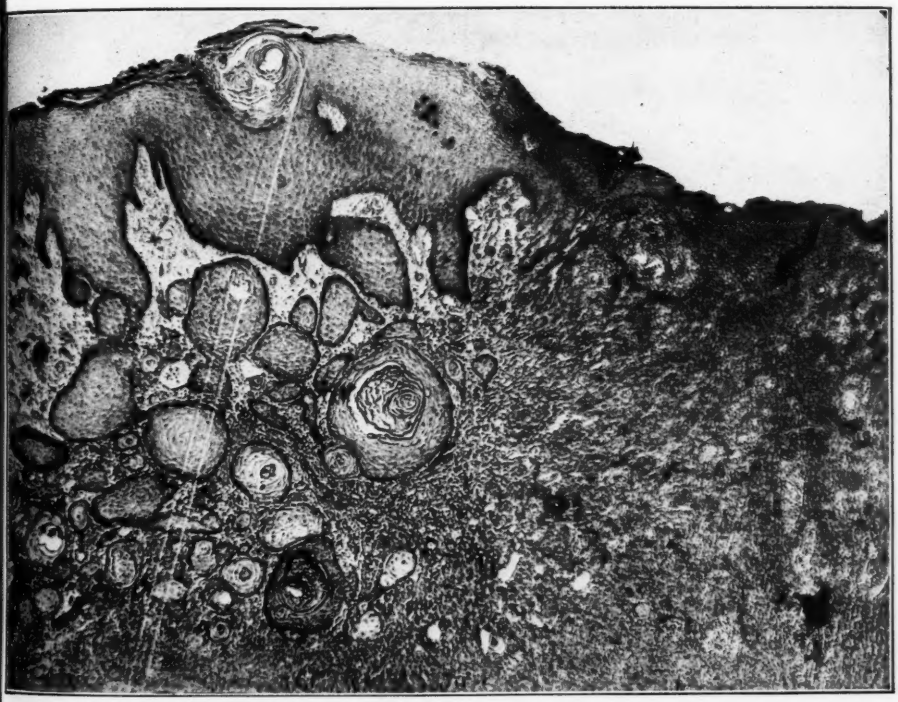

Fig. 2.—Photomicrograph showing pseudoepitheliomatous hyperplasia and ulceration of the adjacent epidermis; × 33.

acanthosis with extension of the rete pegs into the lower portion of the cutis (fig. 2). However, no evidence of anaplasia or carcinoma was noted. The other edge showed ulceration, with a dense infiltrate extending to its surface. The entire

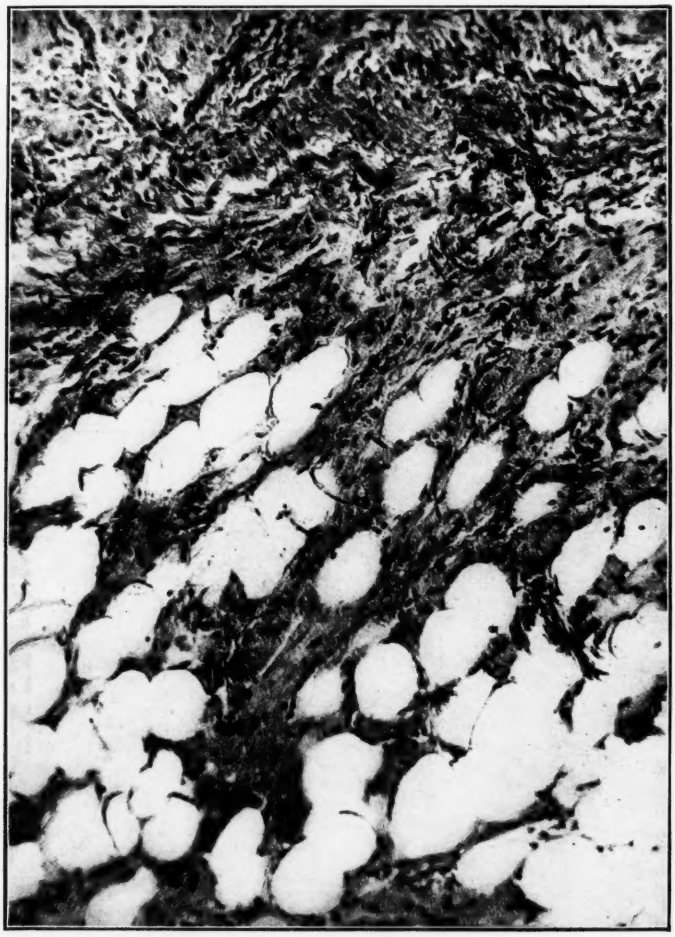

Fig. 3.—Photomicrograph showing infiltration of the subcutaneous fat by tumor cells; × 163.

corium and subcutaneous fat (fig. 3) were invaded by dense nests and cords of large polyhedral cells (fig. 4) containing abundant, coarsely granular, acidophilic cytoplasm, with eccentrically placed, round or oval vesicular hyperchromatic nuclei (fig. 5). Special stains for fat did not reveal its presence.

Fig. 4.—Photomicrograph showing the dense cords of tumor cells in the corium; × 120.

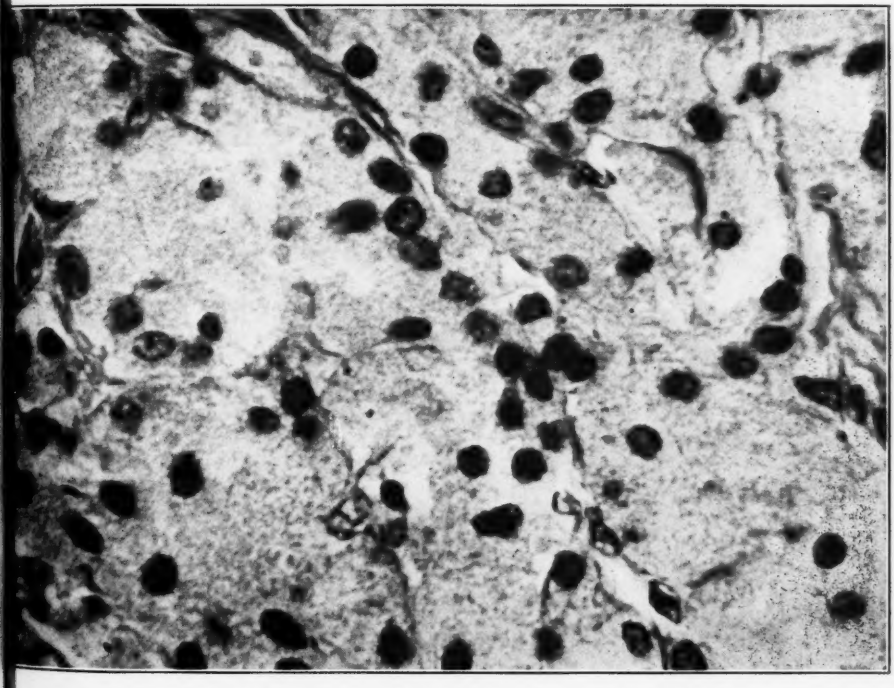

Fig. 5.—High power magnification of the tumor cells; × 862.

COMMENT

This case is of particular interest because of its superficial resemblance to one of granuloma inguinale. This diagnosis was supported by the fact that the lesion had developed in the genital region in a patient with previous venereal disease. However, closer inspection disclosed that the granulomatous ulcer took the form of a truncated cone, which observation is unusual in granuloma inguinale. Nevertheless, the clinical impression necessitated a search for Donovan bodies, which were not found. As far as we are aware, this is the first case of such nature to be reported.

SUMMARY

The clinical and microscopic features of granular cell myoblastoma are reviewed and theories as to its histogenesis discussed.

A case of cutaneous granular cell myoblastoma is reported. The unusual feature of this case was its resemblance to one of granuloma inguinale.

PACHYONYCHIA CONGENITA

Regression of Plantar Lesions on Patients Wearing Specially Made Rubber Base Foot Molds and Shoes

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NEW YORK

AN INTERESTING therapeutic result is herewith reported. A patient with large calluses and bullae on the soles due to pachyonychia congenita was able to walk with comfort immediately on wearing specially fitted rubber base foot molds. There was gradual and steady involution of the lesions so that to the time of writing, except for the flat and diffuse calluses on the heels, only one cherry-sized callus remained on each metatarsal arch. Each of these was also gradually undergoing involution after the depressions in the foot molds corresponding to the sites of these painful lesions had been deepened.

REPORT OF CASES

CASE 1.—*History.*—L. H.,[1] a young man aged 18, was first seen at the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School and the Skin and Cancer Unit of University Hospital on Jan. 23, 1947. His general health had been good. His mother had a similar congenital skin disease, and her case is reported here as case 2. His sister and her child had no such disorders. There was no history of consanguinity of his parents or grandparents.

His mother noticed one week after his birth that the middle finger of his right hand was discolored. Within a month all the nails of the hands and feet became affected. The mother also noticed soon after his birth that his tongue was "coated at all times." A white patch developed on the buccal mucous membranes as his teeth erupted. When he began to walk, very painful erythematous patches appeared on the soles. These patches formed into blisters and then developed into calluses which gradually enlarged. The process had reached its height when the patient was 6 years old and had been the same ever since. He was able to walk only with great difficulty and pain because of these blisters and thick calluses, which were located particularly on the balls of the feet and toes. The hard calluses had to

From the Department of Dermatology and Syphilology, New York University Post-Graduate Medical School, Dr. Marion B. Sulzberger, chairman, and the Skin and Cancer Unit of University Hospital.

1. (*a*) Wise, F.: Pachyonychia Congenita with Keratoderma of Palms and Soles and Leukoplakia Oris, Arch. Dermat. & Syph. **58**:608 (Nov.) 1948; (*b*) Pachyonychia Congenita (Keratosis Palmaris et Plantaris: Dystrophia Unguium and Leukoplakia Oris), ibid. **60**:846 (Nov., pt. 2) 1949. (*c*) Garb, J.: Pachyonychia Congenita with Keratoderma Palmaris et Plantaris, Dystrophia Unguium and Leukoplakia Oris, Considerably Improved by Specially Constructed Rubber Base Foot Molds, ibid., to be published.

be pared with a razor about once a month in order to ease the pain on walking. Because of his dermatosis the patient was unable to go to school from the age of 9 to 17.

Dermatologic Examination.—The patient had extensive, almost symmetric, well defined, yellowish, very thick keratotic lesions on the heels, soles and toes (fig. 1), which were tender. There were no calluses on the hands. The nails of the fingers

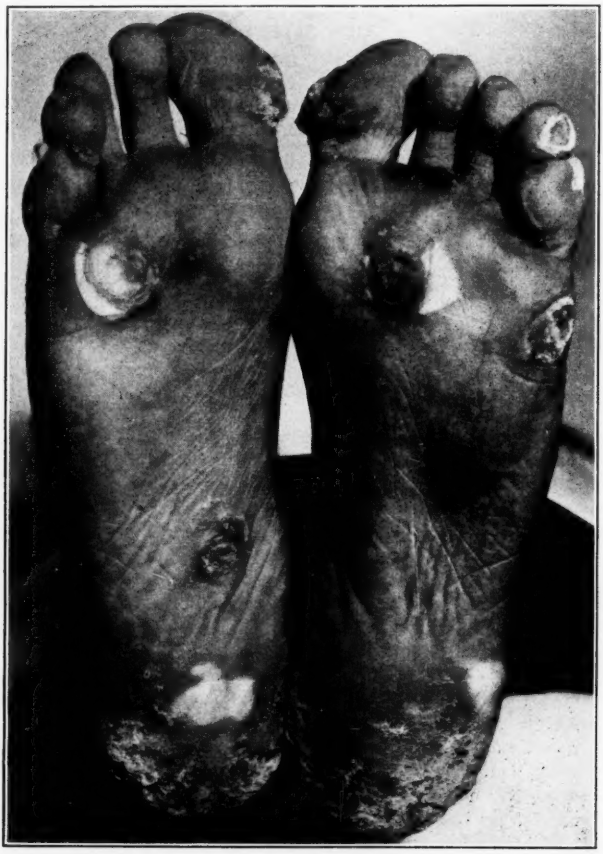

Fig. 1.—Photograph taken on Jan. 23, 1947, showing the calluses on the soles. The lesions on May 25, 1948, before the rubber base foot molds were used were even more pronounced. There were many vesicles and bullae. (The photographs of the nails are shown in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.[1b])

and toes were elongated, curved and discolored. The distal ends were narrowed and some thickened to about 0.5 cm. There were continuous leukoplakic patches on the buccal mucosa along the interdental lines posteriorly, tapering off gradually toward the buccal commissures. The teeth appeared in good condition except for some cavities and fillings. There was gingivitis of the front and sides of the upper

gums. The skin was dry. The patient presented typical keratosis pilaris on the back and lower extremities. The lower part of the back and the lower limbs were covered profusely with black hair. The scalp and hair were normal.

Laboratory Data.—The results of examination of the urine were normal. The hemogram showed hypochromic anemia with an erythrocyte count of 2,850,000. The hemoglobin content was 15.5 Gm. per hundred cubic millimeters, 93 per cent.

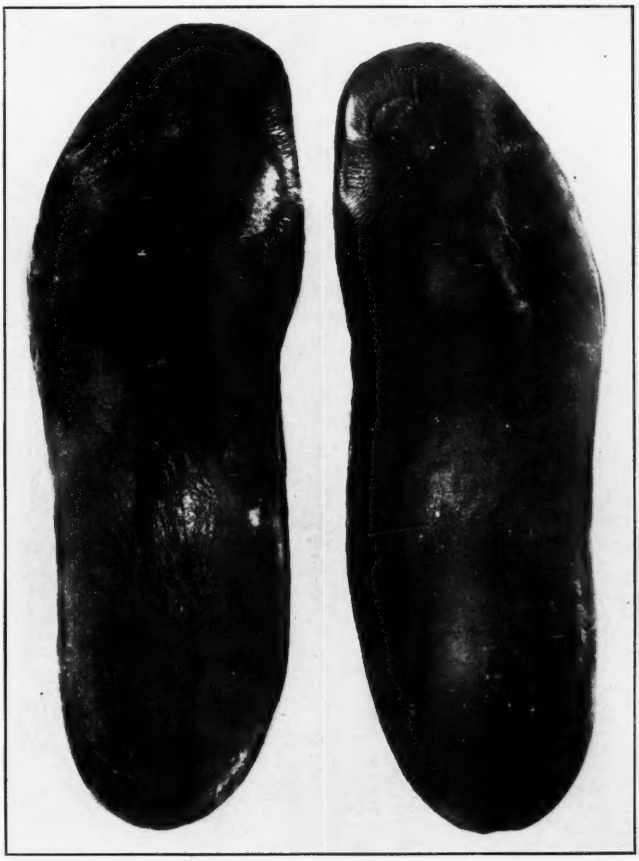

Fig. 2.—The insoles provided for L. H. (case 1).

The color index was 1.2. The leukocyte count was 7,250 cells with a differential count of 55 polymorphonuclear neutrophils and 36 lymphocytes. The Mazzini reaction was negative. The basal metabolic rate was —9 per cent. Total carotenoids and vitamin A content were normal. Eyeground and slit lamp examinations of the corneas did not reveal any observations of significance.

Treatment.—Thyroid extract, ½ grain (0.03 Gm.) once a day, was given concurrently with vitamin A, 25,000 units three times a day, for six weeks until Jan. 23, 1947. From Feb. 19, 1947, to May 25, 1948, the patient took vitamin A

(75,000 units), vitamin E (30 mg.), a preparation containing the vitamin B complex and thyroid extract (¾ grain [0.045 Gm.]) daily. Salicylic acid plaster, 40 per cent, was applied to the calluses on the feet every other day. Resin of podophyllum, 20 per cent, in a vehicle consisting of castor oil, aquaphor® (an oxycholesterol-petrolatum ointment base) and petrolatum, was applied experimentally to two lesions on the soles for one month without any improvement. "Oilzo" [2] was used for six weeks without any noticeable change in the lesions.

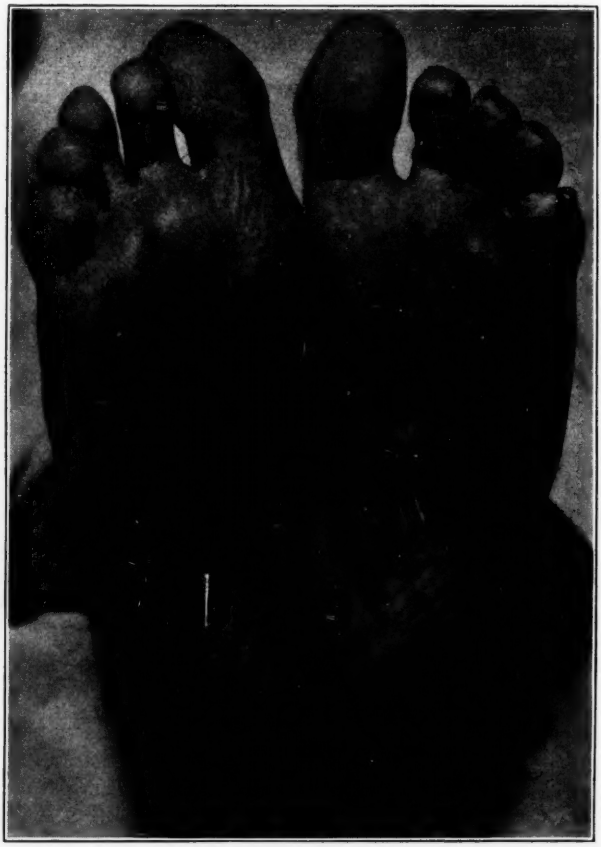

Fig. 3.—Photograph taken May 16, 1949, after the patient had worn the rubber base foot molds for a year, showing the regression of the growths and bullae.

On May 25, 1948, the patient was instructed and began to use specially made rubber base foot molds supporting the entire soles and heels. They were made according to foot prints on which the calluses were outlined. Medium hard resilient

2. A preparation of triolein ozonide in olive oil, liberating oxygen, made by the G. F. Harvey Co., Saratoga Springs, New York. Sharlit, H.: Use of Ozonides in Dermatology, New York State J. Med. **46**:2147 (Oct. 1) 1946.

rubber was used for the base of the molds. The pressure areas were then grooved out of the rubber, cups being formed corresponding to the calluses shown on the foot print. The full molds were balanced to adjust for weight bearing and then were covered with soft pliable leather.

The inner soles of the shoes were also grooved with a hydraulic pressure machine to give greater cupping and procure more freedom from pressure at each severe pressure point. The molds were then set in the shoes and cemented to

Fig. 4.—Photograph taken on Jan. 23, 1947, showing the calluses of the mother, with the callus anterior to the left heel which recurred in the full thickness skin graft taken from the left calf (arrow). The callus in the graft still has a few hairs protruding.

prevent shifting. These molds served the purpose of relieving pressure on the calluses and transferred part of the pressure to the longitudinal arch.

As soon as the rubber molds were used, the patient felt relieved and was able to walk fairly comfortably. By September 1948 three bean-sized and larger calluses on the right sole, a cherry-sized callus on the base of the left little toe and several bullae on the soles had disappeared.

In order that the patient might obtain still greater relief at pressure points new shoes were specially made on Sept. 23, 1948, with enough height to accommodate a mold of at least 3/8 inch (0.94 cm.) in thickness, thus allowing the pressure points to be more deeply hollowed and obviating the necessity of grooving the inner soles of the shoes. The wearing of this pair of shoes resulted in regression of all the lesions except two large protuberant growths, one on the middle third

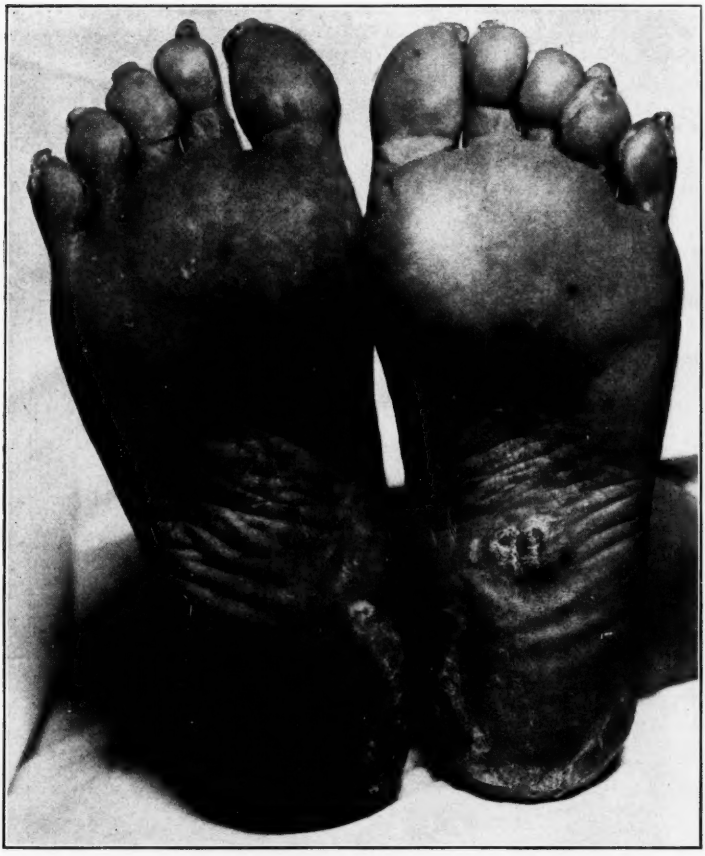

Fig. 5.—Photograph taken on June 6, 1949, just before the rubber base foot molds were given to the patient in case 2, showing improvement over the condition shown in figure 4 as a result of prolonged rest and the patient's staying off her feet.

and the other on the inner third of the right and left metatarsal arches respectively (fig. 3).

CASE 2.—S. H.,[3] the mother of the patient in case 1, suffered from pachyonychia congenita but to a lesser degree than her son. In an attempt to relieve her painful

3. Wise, F.: Pachyonychia Congenita with Keratoderma of Palms and Soles and Leukoplakia Oris, Arch. Dermat. & Syph. **58**:609 (Nov.) 1948; footnote 1b.

and tender plantar calluses she had had a plastic operation performed on the left foot on Jan. 2, 1932, in the orthopedic department of another hospital. A quarter-sized area on the transverse arch of the left sole was excised and a graft taken from the left calf. It was contemplated to graft skin for the entire soles if calluses did not form. However, a large callus, 1.5 cm. circular, developed in this graft within two months (figs. 4 and 5). Some hairs are still present in this graft and even in the callus. When this therapeutic surgical attempt had proved of no avail, the patient was told by the orthopedic surgeon to stay home, relax and keep off her feet.

On May 15, 1947, she was hospitalized at the Post-Graduate Hospital and put to bed. Within six weeks the calluses began to regress, but they recurred again soon after she resumed walking.

On June 10, 1949, she received specially prepared molds and shoes similar to those made for her son. The next day she stated that she could walk with fair comfort. Aluminum chloride solution, 25 per cent in distilled water, was recently prescribed for her to be applied three times a day to the feet for the purpose of counteracting the excessive sweating of the soles, thus enabling her to wear the shoes continuously at home unless she is resting. Tincture of belladonna in 5 minim (0.30 cc.) doses twice a day is occasionally given in addition to the local applications. There has been great and sustained subjective improvement (fig. 5).

COMMENT

Apparently in this congenital anomaly there are inherent weakness and lowered resistance of the skin and mucous membranes to pressure, irritation and friction. Because of these factors and because of the differences in the tissues, the abnormality is manifested clinically at the areas of greatest pressure, as on weight-bearing points of the soles, by calluses and bullae (fig. 1); in areas of irritation, such as in the nails, by hyperkeratotic changes, and in areas of frequent friction, as in the mucous membranes of the mouth and tongue, by leukoplakic patches.

That the susceptibility to callus formation is not limited to or dependent on the local disposition of the skin itself is dramatically illustrated in case 2 by the formation of the hard callus on the left sole in a full thickness skin graft removed from the left calf (figs. 4 and 5).

It seems logical to assume that for the patient in case 2, perhaps because the surfaces of her soles were considerably smaller than were those of her son, the results should be less spectacular. This outcome could be attributed to the smaller size of areas which can be utilized to transfer and distribute the pressure points.

It is obvious that these patients will be obliged to wear these costly, specially constructed molds and shoes for life and that every few months the footgear may have to be adjusted. Nevertheless this method certainly appears worthwhile, as is shown by the ability of the patients to walk with comfort after the molds were used. The younger patient is now a totally transformed young man both physically and mentally and is for the first time able to do a full day's work.

Similar molds with modifications to fit each individual case might be used in treatment of other disabilities of the soles, such as painful exostoses, tender plantar verrucae, acquired calluses that do not respond to treatment, painful systematized verrucous nevi on the soles and perhaps epidermolysis bullosa.

A partial review of the literature, including authoritative books on rehabilitation and orthopedics, failed to reveal that such molds as were fitted to these 2 patients had ever been used before.

SUMMARY AND CONCLUSIONS

Two cases are reported, in a mother and son, of pachyonychia congenita. Large calluses and blisters on the feet of these patients had defied every form of therapy applied and caused them to walk only with great difficulty and with considerable pain. They had to resort once a month to paring down the calluses with a razor. In the first case, that of the son, several calluses and blisters regressed within two months after the patient began wearing specially constructed molds. Further regression occurred later as a result of molds fitted in specially constructed shoes of sufficient height to contain molds ⅜ inch (0.94 cm.) thick. These allowed for deeper grooving so that to date only one callus on each sole remains. These calluses were gradually undergoing regression, at the time of writing, the grooves corresponding to these growths having been deepened. The patient is now able to walk with little discomfort and to work steadily. The patient in case 2, the mother of the patient in case 1, with the same congenital anomaly, was given similar molds and shoes on June 10, 1949. She was able to walk with complete comfort at the time of writing. An additional topical remedy was recently prescribed for her to combat the excessive sweating of the feet, thus enabling her to wear the shoes constantly at home, particularly during the hot weather, as well as on the street.

That the predisposition to callus formation is not a local phenomenon is illustrated in case 2 by the formation of a large callus in the graft taken from the left calf to replace the calloused skin removed from the left sole. A few hairs are still visible in this callus, showing the independent viability of the flap from the calf.

From these observations it appears as though the skin and mucous membranes of patients with pachyonychia congenita may be congenitally weak or defective in their capacity to support pressure, friction and other irritations and inclined to respond to such local trauma with calluses, hyperkeratotic changes in the nails and leukoplakic patches.

219 East Nineteenth Street (3).

Mrs. Bernadette Kelley and the Social Service Department of University Hospital of the New York University–Bellevue Medical Center obtained the funds for the shoes for the mother and son.

ALLERGIC ECZEMATOUS CONTACT TYPE DERMATITIS CAUSED BY COCOBOLO WOOD (DALBERGIA)

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BROOKLYN
AND
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ALLERGIC eczematous contact type dermatitis caused by cocobolo wood has been reported several times, but at infrequent intervals. We have reason to think that sensitization to this wood and clinical episodes from contact with it are commoner than the sparse reports would lead one to expect. Also, we will indicate a rather new source of exposure which we think may make dermatitis of this causation commoner still.

The earliest record we could find of an eruption attributed to cocobolo wood came from abroad. Stern (cited by Levin [1]) in 1891 reported cheilitis in flute players whose instruments had mouth pieces made of this material. In this country MacKee [2] was one of the first to note dermatitis from cocobolo wood. His case was occupational and occurred in a person who scraped the wood in the processing of it for handles and backs of hair brushes. Since then there have been isolated reports of cases resulting from exposures under domestic and avocational circumstances by Abramowitz and Swarts,[3] Levin [1] and Howell.[4] Hollander [5] recorded a case of "knife handle dermatitis" which requires special comment. An eruption of the hands in a person known to be sensitive to lacquer was circumstantially proved, by trials of elimination and reexposure, to be due to a paring knife handle made of a botanically

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School, Dr. Marion B. Sulzberger, chairman, and the Skin and Cancer Unit of University Hospital.

1. Levin, S. J.: Cocobolo Wood Dermatitis: Case Due to Wooden Handles on Kitchen Knives, J. Allergy **12**:498 (July) 1941.

2. MacKee, G. M.: Dermatitis Venenata from Cocobolo Wood, J. Cutan. Dis. **31**:582 (Aug.) 1913.

3. Abramowitz, E. W., and Swarts, S. W.: Dermatitis Due to Cocobolo Wood, Arch. Dermat. & Syph. **37**:441 (March) 1938.

4. Howell, J. B.: Contact Dermatitis: Analysis or Tabulation of All Cases Proved in a Single Year, Arch. Dermat. & Syph. **53**:265 (March) 1946.

5. Hollander, L.: Dermatitis Due to Stain on the Wooden Handle of a Kitchen Knife, Arch. Dermat. & Syph. **43**:381 (Feb.) 1941.

unidentified wood. The allergenic principle was ascribed to a stain which was presumed, but not proved, to be present on the wood. We suspect that this case may have been another instance of dermatitis due to cocobolo wood and not a case due to a stain. A wood was certainly contacted whereas contact with a stain was assumed.

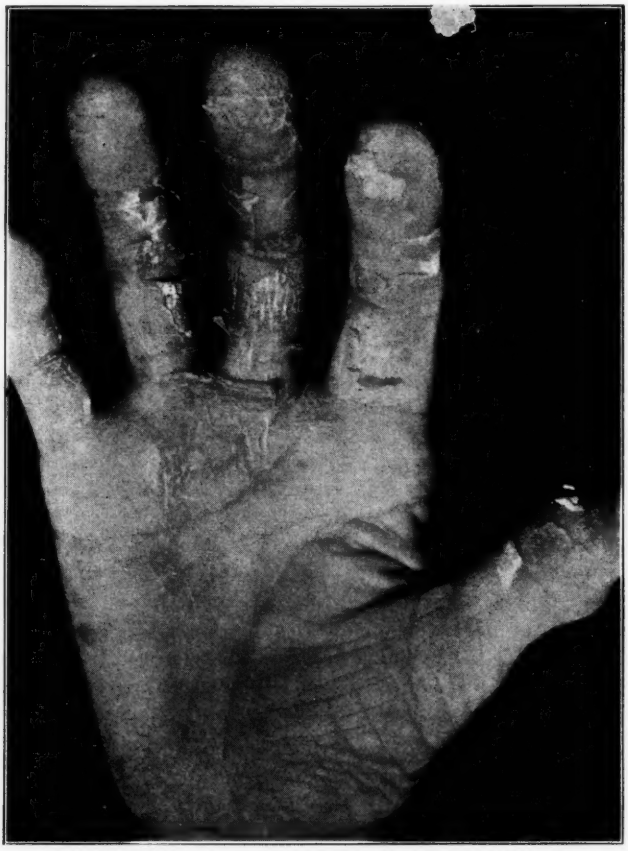

Fig. 1.—Clinical appearance of the eruption seen in case 1 in the involuting phase.

Eczematous eruptions of the hands and lips are among the more exasperating problems dermatologists have to deal with. Etiologic resolution in such cases is frequently difficult, if not impossible, for the physician, and cure is equally troublesome for both doctor and patient. When both etiologic resolution and cure are promptly effected in cases whose causes have threatened to be obscure, the joy is so great that one

is instantly prompted to communicate the "miracle" to one's colleagues. The cases reported here are 2 such wherein solution and cure were accomplished with dispatch because dermatitis was proved to be due to sensitization to cocobolo wood.

REPORT OF CASES

CASE 1.—B. K., a 64 year old housewife, complained of recurrent episodes of a bullous eruption on the right palm over a period of twenty years. Each attack was characteristic and as follows: The palmar surfaces of the proximal phalanges of digits 2, 3 and 4 and the adjacent opposing upper portion of the palm would begin to swell. The tenseness would then spread to the rest of the involved fingers,

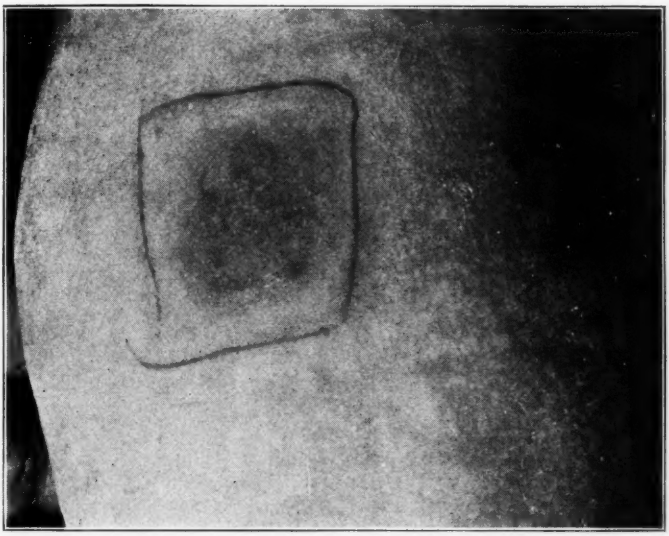

Fig. 2.—Reaction to a patch test with shavings from the handle of a paring knife submitted by the patient in case 1.

and shortly afterward large bullae would cover these areas (fig. 1). Treatment on many occasions consisted of the application of various palliative topical medicaments and roentgen ray therapy. Attacks would eventually end after a variable period of disability, only to recur after short periods of normalcy. On the occasion of the patient's visit to us, this case being the first of the kind under our observation, it occurred to us that the condition might be a contact dermatitis due to sensitization to cocobolo wood from a knife handle or some similar piece of domestic equipment. After we had explained the possibilities to the patient she brought a favored paring knife which we could see was grasped and manipulated in such a manner that the points of contact with the handle fitted exactly the shape, area and extent of the dermatitis. We consequently made patch tests with scrapings from the submitted knife and with shavings from cocobolo wood in addition to many other woods from a special patch testing set of woods in possession of the allergy

section of the Skin and Cancer Unit. The patient was found to be highly reactive (4 plus grade) to both the wood in her knife handle and our cocobolo wood (figs. 2 and 3). There were no reactions to other woods, such as cherry, spruce, teak, mahogany, oak, elm, gum and maple. It is interesting to note that the patch test reactions consisted of large bullae which imitated the clinical eruption exactly.

Fig. 3.—Reaction to a patch test with cocobolo wood done on the patient in case 1.

The dermatitis improved promptly on the patient's avoidance of all kitchen knives with similar wooden handles and had not recurred to the time of writing despite resumption of the patient's use of these knives with their handles well covered with adhesive plaster. It remains to be seen whether such occlusion will be sufficient to contain the allergenic principle in cocobolo wood. We expect, on the basis of other experiences with the remarkable capacity of some allergens to penetrate seemingly

impenetrable barriers [6] that eventually the provocative substance will seep through and tend to cause recurrences.

CASE 2.—E. R., a 30 year old teacher and amateur musician, acquired a musical instrument known as the recorder (fig. 4). After practicing with it for one month, the patient noted swelling of the lips. On the instrument's being put aside the cheilitis quickly subsided, but it reappeared just as quickly on resumption of playing. Again a patch test with scrapings from the instrument, which is known to be

Fig. 4.—Musician demonstrating the playing of the wind instrument known as the recorder.

fabricated from cocobolo wood (manufacturer's statement), gave a strongly positive reaction (3 plus). At the time of writing taping of the mouth piece with adhesive plaster was affording fair protection; some slight pruritus of the lips was felt only after prolonged blowing. The fingers which hold the instrument and

6. Leider, M., and Furman, D.: Allergic Eczematous Contact-Type Dermatitis from Odd Things or in Odd Ways, Ann. Allergy **6**:693 (Nov.-Dec.) 1948.

operate its orifices had not been affected. This patient reported another case of cheilitis in a fellow music student, and the teacher of the class was said to know of still other cases resulting from the contact with the same instrument.

DISCUSSION

Cocobolo wood,[7] known in the trade as "bastard mahogany" is derived from trees that are indigenous to tropical zones, i. e., in the Western Hemisphere, Mexico, Central and South America and the Antilles. Botanically, the tree family is Leguminosae, the genus is Dalbergia and the important species are retusa, hypoleuca, granadillo, calycina and lineata. In its ligneous character, cocobolo is rated a hard wood. It is beautifully grained, red-brown to yellow, heavy and strong. Because of its oil content, it is impervious to water, resists splintering and polishes to a high luster without staining or other special treatment. These qualities make cocobolo wood suitable for knife, fork and brush handles, mouthpieces of some wind instruments, bracelets and other trinkets, policemen's clubs and similar objects. Its drawback is its sensitizing potential, which, as woods go, is probably high.

The whole subject of allergic eczematous contact type dermatitis from woods, in general, is always timely and of great practical importance. Despite modern uses of plastics, wood is now as ever used, industrially and domestically, in tremendous quantities. Occupationally, lumbermen, sawyers, carpenters, cabinet makers and makers of wood instruments, for example, are highly exposed and suffer comparatively frequent sensitization. In the home, handles of kitchen utensils and toilet seats [6] seem to be the commonest sources of exposure and trouble. Wood objects of personal adornment are common causes, too. Ordinary furniture, except possibly wooden arm chairs and desks, is not excessively important in this respect.

In short, wood dermatitis, while well known, needs periodic reemphasis. In the present report is seen an instance of expeditious dealing with a protracted, recurrent, obscure dermatitis of the hand by an awareness of the possibility of wood dermatitis. The discovery of cocobolo wood as a cause of cheilitis in musicians, while more obvious, deserves special note. This wood seems to be returning to favor in the production of wind instruments. The ancient instrument known as the recorder, for example, is gaining in popularity among amateur musicians, and, if the case of our musical patient together with the other cases cited by her are harbingers, many more cases of cheilitis may be expected from this source.

820 Caton Avenue, Brooklyn 18 (Dr. Leider).

7. Most of the botanic data on cocobolo wood was taken from publications of the United States Department of Agriculture (Forest Service).

Clinical Notes

POIKILODERMATOMYOSITIS (POIKILODERMA VASCULARE ATROPHICANS)

Report of a Case Exhibiting Features of Panniculitis, Scleroderma, Periarteritis Nodosa and Calcinosis Cutis

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ST. LOUIS
and
WILFRED E. WOOLDRIDGE, M.D.
SPRINGFIELD, MO.

In recent years there has accumulated a large literature dealing with the interrelationship of scleroderma, dermatomyositis, poikiloderma vasculare atrophicans, disseminated lupus erythematosus, panniculitis, periarteritis nodosa and myositis fibrosa. While these diseases are distinct clinical entities in their typical forms, some specific cases are not typical and show features which may belong to other members of the group, thus making a single diagnosis an impossibility.

At this time there is no agreement on whether or not these diseases have a common etiology or whether their histopathologic and clinical resemblances are only coincidental. Until the problem of etiology is solved one can only speculate and record clinical and pathologic evidence.

Therefore, we present a report of the history and clinical course of a patient who was originally given the diagnosis of dermatomyositis but who later showed also the features of poikiloderma vasculare atrophicans, scleroderma, panniculitis, periarteritis nodosa and calcinosis cutis.

REPORT OF A CASE

H. M., a 23 year old white housewife, presented an illness which had begun in November 1945 when she first manifested swelling and erythema around her eyes and on her cheeks. This had not been preceded by any infectious episode. For two months the erythema was limited to the aforementioned area and the periorbital swelling was often so severe that the patient was unable to see. The erythema then began to spread gradually, and the entire body became involved. During the following month the patient completely lost her eyelashes and eyebrows and axillary and pubic hair and her scalp hair became thin and brittle.

Three months after the onset of her disease her arms and legs became weak and she first noticed that it was difficult for her to comb her hair and to do her housework. These symptoms grew severer during the next few weeks so that she spent most of her time in bed. Soreness of the muscles was present during that time but was never prominent. Amenorrhea developed.

Five months after the onset of her illness she was admitted to the Barnes Hospital, St. Louis, for six weeks and a diagnosis of dermatomyositis was made. By that time she had lost 30 pounds (14 Kg.), she was very weak and her muscles were moderately tender on examination. Her blood pressure was 150 systolic and 100 diastolic, and her pulse rate, 90 per minute. She was afebrile. The laboratory

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and Washington University School of Medicine, service of Richard S. Weiss, M.D., St. Louis.

data at that admission showed mild hypochromic anemia, a sedimentation rate of 1.5 mm. per minute, a basal metabolic rate of + 33 per cent, and a normal electrocardiogram. The diagnosis of dermatomyositis was confirmed by a biopsy of skin and muscle specimens taken from the right deltoid region. During her stay in the hospital the patient was treated with diphenhydramine (benadryl®), neostigmine (prostigmine®), salicylates and spray roentgen ray therapy, all without benefit.

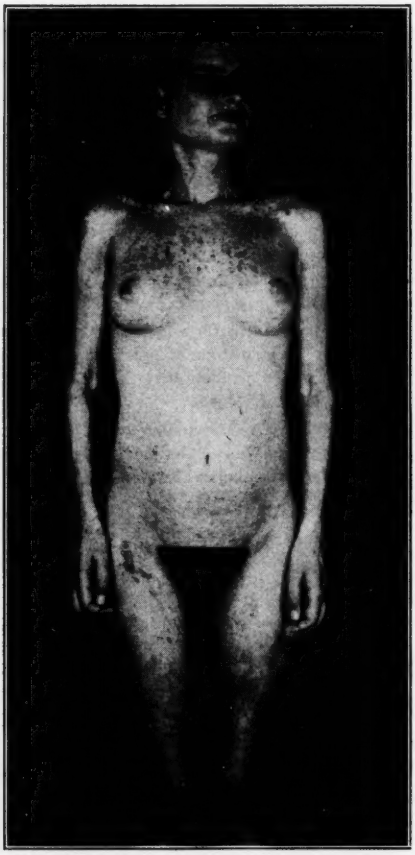


Fig. 1.—The distribution of lesions of the skin.

Seven months after the onset of her disease her skin had become progressively more brownish and scaly and her weakness had increased to the point that she could barely feed herself.

At that time she was admitted to the Barnard Free Skin and Cancer Hospital. Her history revealed no additional information. Her blood pressure was 164 systolic and 110 diastolic. Her weight was 92 pounds (42 Kg.). She had considerable periorbital edema, a moon face and a masklike expression. She could barely

open her mouth but had no difficulty swallowing. She had a constant aortic systolic murmur of moderate intensity. There was no lymphadenopathy. Her muscles were all small, firm and slightly tender. The skin over the entire body was thickened, scaly and showed a dull red erythema (fig. 1). Areas of fine telangiectasia were found over the entire skin surface. Scattered irregularly over the body were many red-brown atrophic macules, 1 to 4 mm. in size (fig. 2). There was no axiliary or pubic hair. The scalp hair, eyelashes and eyebrows were sparse, short and brittle. The tendon reflexes were all present but weak, and the patient volunteered the information that they had been much stronger during her previous admission to the hospital eight months before.

The laboratory data were as follows: blood count, 3,780,000 red blood cells and 8,800 white blood cells with 10 Gm. of hemoglobin and a differential count of 64 polymorphonuclear leukocytes, 14 eosinophilic leukocytes and 22 lymphocytes;

Fig. 2.—Close-up view of left upper portion of the chest and shoulder showing discrete inflammatory lesions.

urine, normal; reaction to Kahn test, negative; basal metabolic rate, + 3 per cent; electrocardiogram, sinus tachycardia; carbon dioxide–combining power, 64 volumes per cent; alkaline phosphatase, 1 Bodansky unit; 9.4 mg. of calcium, 6.2 mg. of phosphorus, 80 mg. of blood sugar (fasting), 19 mg. of nonprotein nitrogen and 6.8 Gm. of total proteins, per hundred cubic centimeters, with 2.3 Gm. of albumin and 4.5 Gm. of globulin; euglobulin, increased; reaction in formol-gel test, positive; icterus index, 14; prothrombin time, 4½ minutes (control, 3 minutes); reaction in cephalin-cholesterol flocculation test negative; cholesterol, 235 mg. per hundred cubic centimeters, and sedimentation rate, 2.1 mm. per minute.

On two occasions during her admission to the hospital the patient had bilateral otitis media. Her temperature, throughout the admission, reached 100 F. almost daily and on a few occasions was higher than 101 F. Local therapy consisted of

application of 5 per cent boric acid ointment. Because it was felt that this was a degenerative disease the patient was given two courses of injections of antireticular cytotoxic serum [1] with a month between courses. From these she seemed to derive a feeling of well-being and some increase in strength but no alteration in her temperature and no visible change in the skin. Two weeks after the completion of the second course of antireticular cytotoxic serum it was noted that she had firm, granular, whitish plaques in the antecubital (fig. 3) and popliteal spaces, the anterior axillary lines, the medial surfaces of the thighs and the labia majora. These all appeared simultaneously and were first noted by the patient because they were tender. These plaques gradually increased in size for three weeks and then remained stationary. The antecubital plaques occasionally ulcerated and discharged chalky granules. Six weeks after her last injection of antireticular cytotoxic serum the patient was started on treatment with a course of tripelennamine (pyribenzamine®) hydrochloride, 50 mg. every four hours, but this was discontinued because of side reactions. She then received intravenously administered

Fig. 3.—Roentgenograms of soft tissue of elbows, showing antecubital calcification.

typhoid vaccine fever therapy on three occasions at intervals of three days. After this treatment the patient was discharged from the hospital in a considerably improved condition.

After eight weeks she was again admitted to the hospital. It was at once apparent that she was much improved; she could perform physically with greater freedom; she had gained 7 pounds (3 Kg.) in weight, and her hair showed regrowth in all areas. Menses had again become normal. The calcified plaques were practically unchanged. The skin was essentially the same although the degree of edema was diminished. The blood pressure remained elevated, but the pulse rate was normal. Blood counts were within usual limits. The sedimentation rate remained high at 0.6 mm. per minute but was considerably reduced from its former level.

Since her second hospitalization the patient's improvement has been slow but continuous. The skin is now less thickened and erythematous and shows no scaling.

1. The antireticular cytotoxic serum was supplied by the Lilly Research Laboratories, Eli Lilly Company.

Telangiectasia and atrophy are still present, but less prominent. The patient is afebrile and has gained in weight. She does her own housework except that she experiences some difficulty in stooping and bending. She became pregnant in January 1948, twenty-six months after the onset of her disease, and was delivered of a healthy, 8 pound (3,629 Gm.) female infant on Oct. 5, 1948. The delivery was uncomplicated. After delivery her general appearance was improved and the only positive observations other than residual damage to the skin were a reaction in the thymol turbidity test of 19 units and a 1:1 albumin-globulin ratio with a normal level of total serum proteins.

The report on the pathologic picture was as follows:

1. In a section of skin and muscle from the right deltoid region, taken in April 1946, during the patient's admission to Barnes Hospital, the changes were reported as those of dermatomyositis.

2. In a section of skin from the left antecubital space, which included a hard, white plaque, taken in May 1947 during the patient's first admission to the Barnard Free Skin and Cancer Hospital (fig. 4 *A*), the epidermis showed slight hyperkeratosis and an increase in the granular layer. The prickle cell layer was thinned in some areas, being only three to four cells in depth, and the nuclei were flattened and elongated. The basal cell layer was disorganized in some areas.

In the superficial part of the cutis the capillaries were dilated and surrounded by a moderate number of round cells. The chromatophores were increased in number and were filled with brown pigment. Large amorphous masses of basophilic material (calcium), about which there were evidences of capsule formation, were found in the upper portion of the cutis, and the midcutis. The elastic tissue was fragmented.

These changes were compatible with the picture in poikiloderma chronica atrophicans and in calcinosis cutis.

3. In a section from the skin, subcutaneous tissue and muscle of the right deltoid region, taken in May 1947 during the patient's first admission to the Barnard Free Skin and Cancer Hospital, all tissues were affected to a varying degree, but the structures most involved were the blood vessels in the subcutis and the muscle tissues (fig. 4 *B*).

In some areas the epidermis was thinned and the basal cell layer was washed out. The capillaries were dilated and were surrounded by a mild infiltrate of round cells. In some parts there was interstitial edema of the collagen; small vesicles containing fibrin and a few round cells were formed, and these were limited by the epidermis above. In other areas the collagen fibers were swollen and pressed together to give a somewhat homogeneous appearance. About the appendages were infiltrations of round cells.

The subcutis was decidedly involved. The blood vessels were choked with round and plasma cells and were so altered that it was difficult to recognize their various parts. The blood vessel lumens were obliterated (fig. 4 *C*). The infiltrate extended into all layers of the fat and in some places replaced the normal architecture of the fat.

Similar pronounced changes were apparent in the muscle layer. The muscle parenchyma showed destructive changes, and the transverse bands of the fibers were not seen (fig. 4, *D* and *E*). It was almost impossible to identify this material as muscle tissue. The blood vessels of the muscles were affected in a fashion similar to that affecting the fat but to a lesser degree. The infiltrate of round and plasma cells extended between the remnants of the muscle bundles.

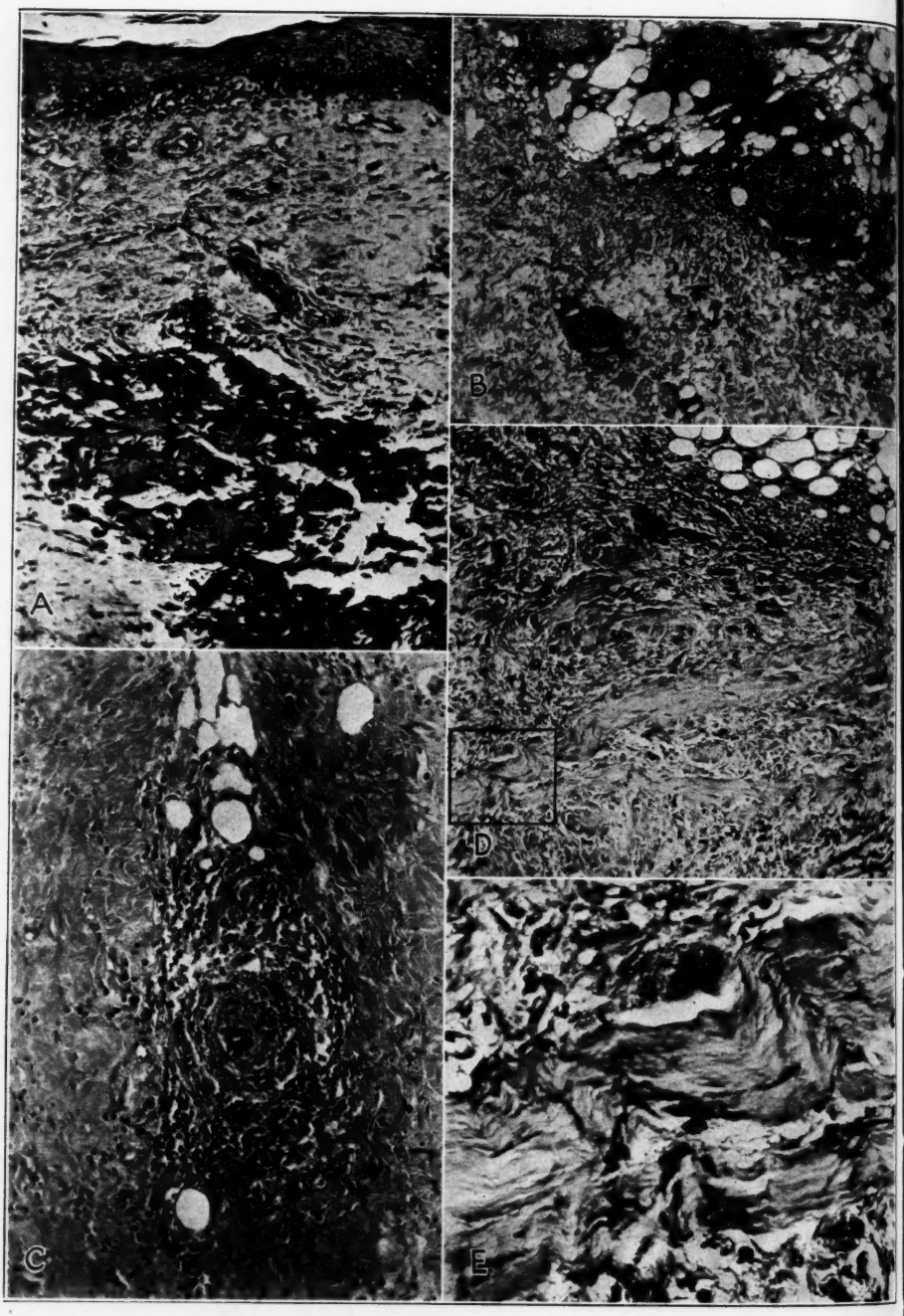


Fig. 4.—*A*, section of epidermis and cutis from left antecubital fossa, showing changes of poikiloderma chronica atrophicans and deposits of calcium in the cutis; hematoxylin and eosin, × 55. *B*, section of the subcutis and muscle from the right deltoid region. The blood vessels are gorged and are surrounded by a dense infiltrate. The architecture of the fat and muscle is destroyed; hematoxylin and eosin, × 30. *C*, section of blood vessel in muscle tissue. The structure of the vessel is almost completely destroyed and the lumen obliterated. There is a heavy infiltrate of round and plasma cells; hematoxylin and eosin, × 183. *D*, section of muscle. The bundles are disorganized and destroyed and resemble strands of collagen; hematoxylin and eosin, × 103. *E*, inset of *D* showing individual muscle fibers. The cross striations cannot be seen; hematoxylin and eosin, × 550.

These changes were compatible with those of dermatomyositis, panniculitis, periarteritis nodosa and a mild degree of scleroderma.

COMMENTS

The young woman in the case reported had severe involvement of striated muscle, collagen, blood vessels, fat and epidermis. There seems to be no doubt that the evident disease in this patient was dermatomyositis. It is logical to assume that the changes in the other tissues were produced by the same agent which caused the dermatomyositis since the entire disease picture emerged coincidentally. In view of the diversity of the tissues involved it seems probable to us that these changes were achieved by means of blood vessel damage.

In the past, opinions have differed as to whether poikiloderma vasculare atrophicans (Jacobi) is a true clinical entity or whether it is a complex arising from damage to the epithelium and subjacent tissues. Since the clinical and histologic pictures produced in this case approximate a true poikiloderma vasculare atrophicans so closely, one is led to conjecture whether or not it is the same type of poikiloderma vasculare atrophicans which is seen alone. The same questions are thus raised in regard to the remaining disease complexes manifested in this patient and in this disease group. After prolonged observation we can assume only that all the changes found in this patient were but the products of a single process. We also feel that at least poikiloderma vasculare atrophicans and dermatomyositis may be caused by the same or by similar agents.

We cannot determine whether the pronounced improvement in the condition of this patient following the use of the antireticular cytotoxic serum and typhoid vacine was due to either or to both of these agents or whether the patient entered into a spontaneous remission at that time. We feel, however, that the trial of these agents in treatment of this disease group deserves further attention.

SUMMARY

A case of poikiloderma vasculare atrophicans in which were exhibited lesions of calcinosis cutis is reported. Also there were microscopic features of scleroderma, panniculitis and periarteritis nodosa.

The patient entered a period of remission after treatment with antireticular cytotoxic serum and typhoid vaccine.

100 Professional Building, Cherry and Kimbrough Streets, Springfield, Mo. (Dr. Wooldridge).

KERATOSIS FOLLICULARIS

Report of a Case with Linear Arrangement of Lesions Limited to the Right Lower Extremity

HARRY M. ROBINSON Jr., M.D.
BALTIMORE

In most of the cases of keratosis follicularis which have appeared in the literature since Darier's description in 1889[1] there was involvement of the scalp and trunk.

From the Department of Dermatology, University of Maryland School of Medicine.

1. Darier, J.: Note sur l'anatomie pathologique de la maladie dite psorospermose folliculaire végétante à propos d'un cas nouveau, Ann. de dermat. et syph. **7**:742, 1896.

The following case is presented because of the unusual distribution of the lesions and the limitation of the disease to the involved extremity.

REPORT OF A CASE

V. B., a married white woman, aged 30, was first seen by me on Feb. 1, 1946, with the complaint of an eruption on her right leg of seven years' duration. Two months prior to the onset of these lesions the patient had had a severe sunburn. Shortly after the peeling of the skin from the sunburn had completely exfoliated, lesions had appeared on the right thigh and leg. The patient had gone to several physicians, who had prescribed various ointments, none of which had given her any relief. There were no subjective symptoms, but the presence of the lesions was

Fig. 1.—Note linear arrangement of verrucoid lesions on the lateral aspect of the right thigh and leg. These were the only lesions present.

quite disturbing. After several years of futile attempts to be rid of the eruption by topical applications she had gone to a physician who had removed the lesions by desiccation. The lesions had recurred at the margins of the scar and formed a band extending down the outer surface of her right thigh. Her general health had in no way been impaired since the onset of the lesions. She had been pregnant three times and each time had had a normal healthy child, none of whom had any cutaneous defect. Her past history and review of the systems were noncontributory.

Physical Examinations.—The patient was observed to be a young white woman aged 30, in no acute distress. The general examination of her head, eyes, ears, nose, throat, chest and abdomen revealed no gross abnormalities. The skin lesions (fig. 1) were confined to the right thigh and leg and extended from the anterior

superior spine of the ilium down the lateral surface of the thigh and leg to the ankle. There were several scattered superficial, well healed scars which ranged from 1 to 1.5 cm. in diameter. These groups of lesions formed an irregular band 2 to 3 cm. in width from the anterior superior iliac spine to the right lateral malleolus. At the margin of each of the scarred lesions there were hyperkeratotic, verrucoid papules measuring 2 to 3 cm. in diameter. The verrucae-like lesions were soft, friable and easily removed without the production or the exposure of any bleeding points. Elsewhere in this band there were numerous verrucoid hyperkeratotic papules forming patches 1 to 1.5 cm. in diameter. The keratoses were friable, soft and somewhat greasy. They were easily removed by rubbing and on removal left

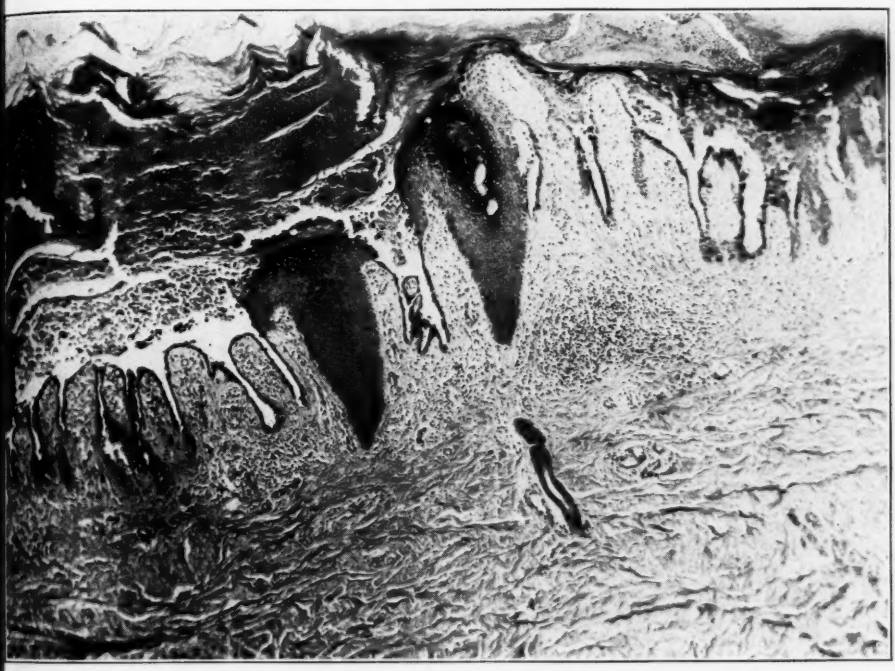


Fig. 2.—Low power view of section of skin showing characteristic "basket weave" arrangement of stratum corneum and lacunas in the rete.

no bleeding points but an irregular, dry, hyperkeratotic base. There were no lesions elsewhere on the body. The results of urinalysis were completely normal. The complete blood picture showed no abnormality.

Histopathologic Observations.—The specimen was taken from one of the lesions on the lateral border of the right leg. There was pronounced hyperkeratosis extending the entire length of the specimen. There was a spotty but well marked parakeratosis and some "basket weave" arrangement. In some areas there was complete degeneration of all the layers of the epidermis superficial to the basal layer; however, this layer remained intact throughout the length of the specimen. In other areas there was an irregular acanthosis. There were numerous places

in which a space existed between the basal layer and the rest of the epidermis. Many of the cells bordering on these spaces had doubly refractile membranes (fig. 2). In the areas where the superficial layers of the epidermis had undergone degenerative changes these cells were particularly prominent. Also in these areas grains were noticed. There was a mild perivascular infiltrate of round cells, plasma cells and occasional epithelial cells which occurred in the upper layer of the cutis. The infiltrate was not distinctive. On the patient's first visit a biopsy specimen was taken and, after the study of the section, treatment was instituted as follows: The patient was given vitamin A in doses of 100,000 units twice daily and a prescrip-

Fig. 3.—High power view of a portion of the section shown in figure 2, showing numerous "corps ronds."

tion for a 10 per cent salicylic acid ointment. It was hoped that application of this ointment would remove the keratotic lesions. This treatment was employed for a period of three months. After this the patient was given fractional doses of roentgen rays, 50 r to the involved areas for ten successive weeks. As there was no improvement after this therapy, it was decided then to remove the lesions by superficial desiccation. Several small areas were removed on each visit with the use of light desiccation until all the lesions on the right leg had been completely removed. Six months after removal of all the lesions the verrucoid areas had been replaced with soft scar tissue and there had not been a recurrence of any activity.

COMMENT

Although the distribution of lesions in this case was unusual, the clinical features of the eruption and the histopathologic picture were characteristic. Because of these features it was thought that a report of this case merited publication.

1025 North Calvert Street.

CHAPPING OF THE SKIN ON RETURNING FROM THE TROPICS TO A COOLER AREA

HERMAN V. ALLINGTON, M.D.
OAKLAND, CALIF.

World War II taught dermatologists that numerous diseases of the skin became worse in tropical and subtropical climates. It is not so generally realized that the skin may also suffer when a person returns from the tropics to a cooler and drier climate.

During the war in military personnel newly returned to the usually cool San Francisco Bay region from the warmer Pacific areas occasionally dermatitis developed. This appeared to be identical with, but often more acute and severer than, the pruritus hiemalis, or "winter itch," which is seen during the fall and winter months in temperate climates.

Since the war the same skin condition has been noted in civilian practice. It is probable that with the continued development of our Pacific Island bases and with increasing travel to the South and the Orient this dermatitis will be seen more frequently. It is characterized by dryness, redness and scaling. Vesiculation does not usually occur, but in severer cases the epidermis becomes superficially fissured and eroded and oozing and crusting take place. The condition develops in oval or irregular patches of varying sizes with ill defined margins. These patches may become confluent and cover large areas. The eruption tends to be symmetric in distribution. It involves primarily the hips, buttocks, thighs and shoulders and the lateral and extensor surfaces of the arms. Involvement of the trunk, forearms and legs is less frequent. The moister flexural areas are spared.

Two patients recently observed illustrate this problem. Both were middle-aged white men. The first was a construction worker who had returned in mid-summer from Guam, where he had been employed for approximately six months. He had had no trouble with his skin while there, but this characteristic eruption had developed promptly on his return to his home in Oakland. It involved the shoulders, arms, hips and thighs; however, the eruption cleared readily. The second patient was a businessman who had lived for several years in Honolulu, Territory of Hawaii. He had had no skin trouble while there. He returned from the Hawaiian Islands in August, and, within a week or two an eruption began to develop which persisted and became worse until he was seen in November. He had this dermatitis in a severe form, generalized except for the face, hands,

feet and moist flexural areas. He had undoubtedly aggravated it by frequent vigorous bathing and by poorly chosen self treatment. It cleared slowly under treatment over a period of about two months.

It seems that after a person has been in the tropics for some time his skin becomes conditioned to a warm, moist atmosphere. On return to a cooler, drier area, some time may be required for the sebaceous and sweat glands to readjust their activity and for the skin again to become normally moist, soft and pliable.

The change from light cottons worn in the tropics to heavier, coarser, and perhaps woolen, clothing may sometimes contribute to this irritation. Frequent hot soapy baths are likewise often an additional aggravating factor. A person's skin in the tropics may tolerate frequent baths but may rebel when this habit is continued in a temperate area.

This dermatitis has frequently been confused with other skin diseases, especially fungus infections and scabies. The usual medicaments prescribed for infections or parasitic diseases add further irritation to the already inflamed skin.

Treatment should be directed toward soothing and protecting the skin. Baths should be taken infrequently and use of soap and hot water avoided. Soft, long, loose, white cotton underwear (pajamas) may be worn to protect the skin from rough or woolen clothing. Cold cream, hydrous wool fat, petrolatum or other bland oil or ointment should be used locally. Gradual tanning with ultraviolet rays appears to be helpful, and in cases with marked eczematization roentgen irradiation speeds clearing.

SPONTANEOUS ABSORPTION OF EAR LOBULES IN DISCOID LUPUS ERYTHEMATOSUS

LESTER HOLLANDER, M.D.
AND
FRANCIS J. KRUGH, M.D.
PITTSBURGH

We have observed in 2 patients presenting undisputable objective signs of active disseminated discoid lupus erythematosus of the face spontaneous absorption of both ear lobules without evidence of the disease at their site.

REPORT OF CASES

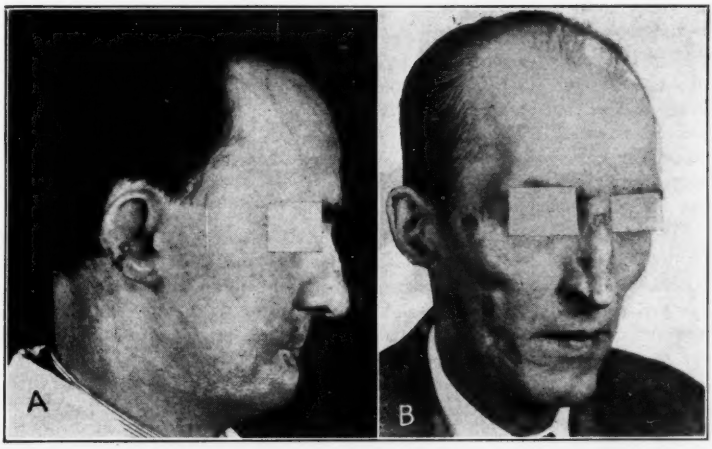
CASE 1.—B. M., an unemployed man, 54 years of age, was referred to the Pittsburgh Skin and Cancer Foundation on June 25, 1937, by Dr. L. E. Etter, of Warrendale, Pa., because of an ulcer of the lower lip of six months' duration and both healed and active lesions of discoid lupus erythematosus of the cheeks, nose, chin and neck. These lesions were of twenty years' duration. He received both local and systemic treatment (salt-free diet, injections of gold salts) without any noticeable benefit.

From the Pittsburgh Skin and Cancer Foundation.

Biopsy of the ulcer of the lower lip proved the lesion to be an epidermoid carcinoma. It was treated with massive doses of unfiltered roentgen rays directed to the carcinoma-bearing area. The ulcer healed; subsequently, after a block dissection of the submental and submaxillary glands and lymph nodes, the patient died of postoperative shock.

The absence of ear lobules was noted by one of us (L. H.), and the patient commented that they shrank away spontaneously and without showing any external evidence of discoid lupus erythematosus We paid no further attention to this phenomenon and merely photographed the patient.

CASE 2.—C. B., a 25 year old mechanic, was referred to the Pittsburgh Skin and Cancer Foundation on Aug. 1, 1934, by Dr. Herbert Frankenstein, of Pittsburgh, because of disseminated discoid lupus erythematosus of the face of three years' duration. He was photographed. He was treated with both local and systemic



A (case 1), absence of ear lobule. The ulceration was not caused by discoid lupus erythematosus. *B* (case 2), the patient in 1949. The discoid lupus erythematosus has progressed. Note the absence of the ear lobule.

measures for about one year without benefit; he then sought treatment elsewhere. He returned to the Pittsburgh Skin and Cancer Foundation on Feb. 8, 1949, because of the appearance of an enlarging hard lymph node in the submental area. The absence of the ear lobules was noted. Comparison with the former clinical photograph, taken in 1934, made the observation more striking.

There have been no lesions of discoid lupus erythematosus on the ear lobules at any time.

SUMMARY

Photographs of absorption of the ear lobules not attributable to local effects of discoid lupus erythematosus are presented. The absorption occurred in 2 male patients. Further observation may prove this to be one of the rare and hitherto unnoted clinical manifestations of disseminated lupus erythematosus.

631 Jenkins Building.

3401 Fifth Avenue.

OFFICE DIAGNOSIS OF SCABIES

J. B. HOWELL, M.D.
DALLAS, TEXAS

Few procedures in the practice of medicine are more impressive to the patient than the personal demonstration of the causative agent of his disease. This demonstration should be done in the majority of cases of scabies. There is a sizable group of people, however, with atypical or minimal scabies for whom the clinical diagnosis is uncertain; for this group, suspected of having scabies, laboratory confirmation is most welcome and helpful. Friedman [1] has correctly stressed that proving the diagnosis in cases of minimal scabies gives the physician and patient assurance and confidence in the correctness of the diagnosis. Proof of the diagnosis when possible is preferable to a therapeutic test with an acaricide.

The patient who doubts the diagnosis of scabies at first is easily convinced when he has viewed the offending mite microscopically. More frequently he will accurately and willingly carry out the treatment for himself and family members if a positive diagnosis can be made. Drug eruptions, Hodgkin's disease, leukemia and other lymphoblastomas, rat and avian mite dermatitis, pediculosis, dermatitis herpetiformis and other conditions which can simulate scabies can be dropped from the differential diagnosis when the organism is found.

By comparative evaluation the dermal curet [2] has been found to be a more satisfactory instrument for obtaining material rapidly and efficiently from suspected lesions than (1) a scalpel with a spearpoint, curved or ordinary type of blade, (2) a razor blade, (3) a pair of scissors or (4) a hatpin or needle with or without magnifying devices. The curet has been found especially satisfactory in recovering the acarus from infants and children.

TECHNIC OF THE LABORATORY TEST

Selection of the Proper Lesion.—The physician should search for and select the freshest primary lesion possible for scraping. The acarus can be demonstrated much more frequently, more readily and more easily from the following anatomic sites: the hands—i. e. the sides of the fingers and the webs—the flexural surfaces of the wrists and the palms and soles of infants. Although the procedure causes more pain in the region of the male genitalia, the mite can usually be easily found in material from papular lesions in this area. Little difficulty is encountered in demonstrating the organism when papular lesions on the axillary folds, umbilicus and nipple sites are curetted. One finds that there is increasing difficulty in demonstrating organisms from the papules on the buttocks and more so from lesions involving the elbow sites. Crusted, infected and irritated lesions should not be scraped if more desirable papules or burrows can be found.

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1. (*a*) Friedman, R.: Atypical Scabies: Diagnosis by the Scrape and Smear Method, Pennsylvania M. J. **47**:39 (Oct.) 1943; (*b*) Biology of the Acarus Scabiei, with Its Early and Recent History, Historia Medicinae Series, New York, Froben Press, Inc., 1942.

2. Carpenter, C. C.: A Rapid Technique for the Diagnosis of Scabies, U. S. Nav. M. B. **48**:566 (July-Aug.) 1948.

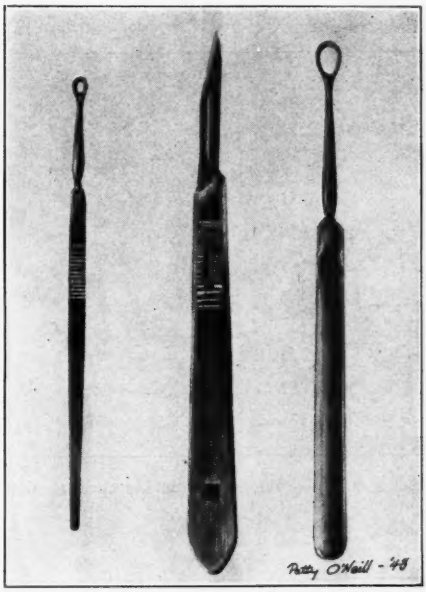


Fig. 1.—Spearpoint scalpel with two types of curets found most serviceable.

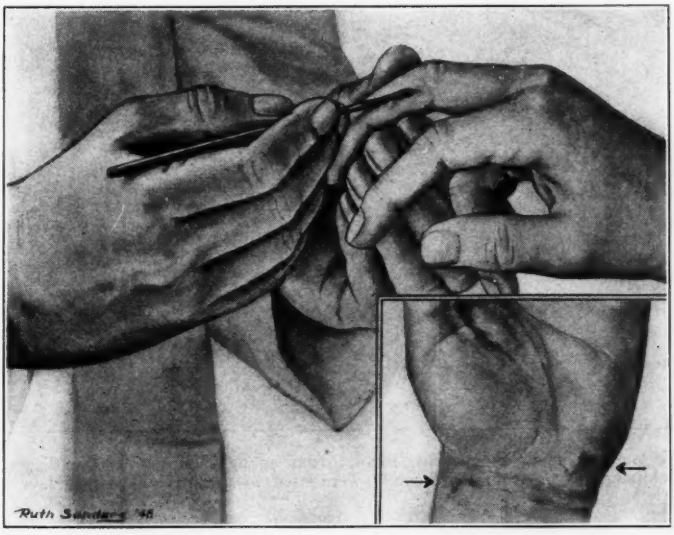


Fig. 2.—Technic of superficial curettage of burrows; insert, exaggerated pattern of burrows on wrist.

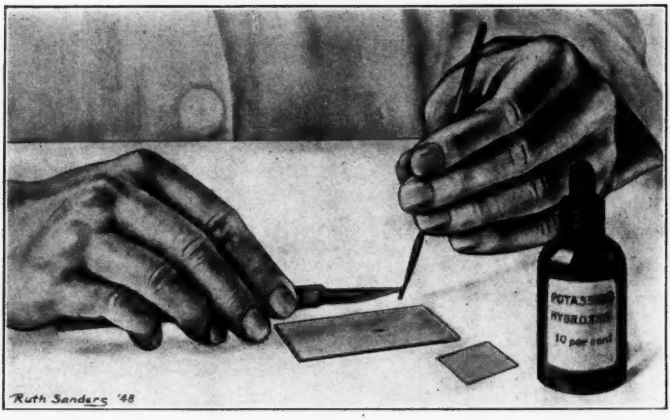


Fig. 3.—Material is carefully removed from the curet to slide with scalpel.

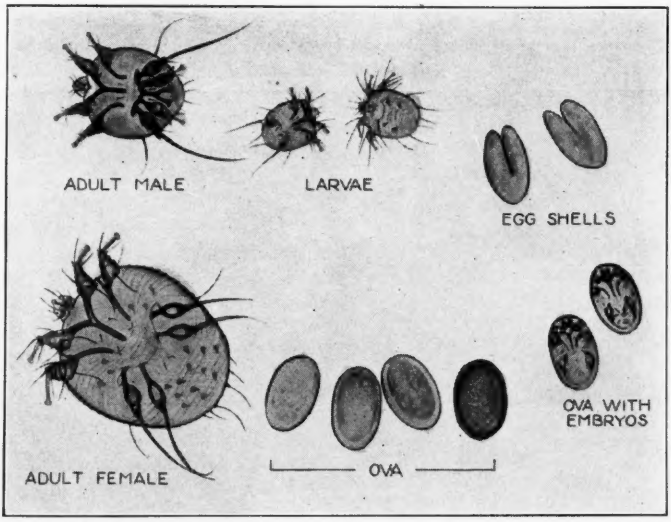


Fig. 4.—Finding the acarus, larva, ovum or eggshell proves the diagnosis. Photomicrographs from Friedman [1b] were used to prepare this drawing.

Technic for Scraping the Burrow or Papule.—A dermal curet (fig. 1) is selected. The skin is held taut between the fingers of the left hand. Very superficial curettement in the direction of the long axis of the burrow or across the summit of a papule is carried out (fig. 2).

Removal of Material from the Curet.—The curettings are immediately deposited on a clean slide. Removal of the specimen from the curet can be aided by a spearpoint Bard-Parker scalpel (fig. 3). One or two drops of 10 to 15 per cent potassium hydroxide solution is placed on the curettings, and a cover slip is applied. Time is allowed for the potassium hydroxide solution to digest the bit of tissue. Gentle pressure on the cover slip results in a thin preparation ready for microscopic examination.

PROOF OF THE DIAGNOSIS

Proof of the diagnosis consists in the finding of the adult female or, less frequently, the male acarus, one or more larval or nymphal forms of the mite, one or more ova with or without embryos or even empty eggshells (fig. 4).

News and Comment

GENERAL NEWS

Specialists Certified by the American Board of Dermatology and Syphilology.—At examinations held in April the following candidates were found proficient and are now certified as specialists by the American Board of Dermatology and Syphilology: Robert R. Allington, Oakland Calif.; Robert A. Bruce, South Pasadena, Calif.; William R. Bundick, Baltimore; Hyman J. Burstein, Decatur, Ill.; Benjamin J. Chester, Brooklyn; Joseph L. Cirincione, Schenectady, N. Y.; Irving Cohen, Flushing, N. Y.; Joseph Copeland, Oakland, Calif.; J. Hughey Crooks, Greenville, S. C.; Walter F. Edmundson, Silver Spring, Md.; Harry H. Fox, Cincinnati; David C. Frisch, Minneapolis; Aaron L. Goldberg, Chicago; John Groopman, New York; Benjamin A. Gross, Philadelphia; Earl S. Hallinger Jr., Cleveland; Lawrence K. Halpern, St. Louis; Morton Hecht Jr., Great Neck, N. Y.; Robert S. Higdon, San Francisco; Victor R. Hirschmann, Fort Sam Houston, Texas; Stephen F. Horne, Rocky Mount, N. C.; Edward G. Jeruss, White Plains, N. Y.; Mark M. Kroll, Cumberland, Md.; Manuel P. Landman, Washington, D. C.; Walter J. McDonough, Wollaston, Mass.; Carter L. Marshall, New Haven, Conn.; Margaret Maynard, Knoxville, Tenn.; William N. New, Great Lakes, Ill.; Laurence L. Palitz, New York; Alvin J. Paulosky, Newport, R. I.; Abraham I. Perley, Birmingham, Ala.; Arthur C. Ressmann, San Antonio, Texas; William Saunders, Watertown, N. Y.; Fred S. Seligmann, Union City, N. J.; Edward E. Shapiro, Bayonne, N. J.; Arthur S. Spangler, Boston; Irving Swartz, Syracuse, N. Y.; Claude B. White, San Antonio, Texas; Arthur P. Wilson, Buffalo, and Louis Zlatkin, Detroit.

The dermatologists in the following list also passed the examination and will become certified specialists after they have completed five years in the specialty: Manuel F. Allende, San Francisco; Woodland W. Anderson Jr., Newport News, Va.; Meyer Berke, Van Nuys, Calif.; Boynton H. Booth, St. Louis; Vincent P. Burby, Pittsburgh; Francis P. Coombs, Brooklyn; Alexander A. Eisenberg, Dallas, Texas; Ynez D. Eskelson, Salt Lake City; Walter C. Fitzgerald, Charlottesville, Va.; Marshall L. Follo, Ann Arbor, Mich.; William H. Fritzemeier, Wichita, Kan.; Donald L. Fuhrman, Kansas City, Mo.; Robert W. Goltz, Minneapolis; Maxwell M. Goodman, New York; Melvin L. Grais, Minneapolis; John W. Hilliard, Pomona, Calif.; Royal E. Ihrke, Chicago; Robert E. Jenkins, Indianapolis; Lyndon M. King Jr., Sioux Falls, S. D.; Philip R. Latta, Chicago; Warren L. Macaulay, Fargo, N. D.; Irving L. Milberg, New York; Primo P. Mori, Hazleton, Pa.; Philip H. Prose, Brooklyn; Milton S. Ross, Brooklyn; Raphael Ross Jr., New Orleans; Allen A. Small, Toronto, Ontario, Canada; Robert H. Snapp, Phoenix, Ariz.; Bartholomew J. Spence Jr., Rochester, Minn.; Douglas P. Torre, New York; Laurence J. Underwood, Glendale, Calif.; Craig Williamson, Pasadena, Calif., and Lawrence M. Zell, Little Rock, Ark.

Examinations by the American Board of Dermatology and Syphilology.—The next written examination by the American Board of Dermatology and Syphilology is scheduled for September 14 in various cities throughout the United States. The oral examinations will be given in Detroit, October 20 to 22. The last date for receiving applications is July 1.

Obituaries

JOSEPH GRINDON Sr., M.D.

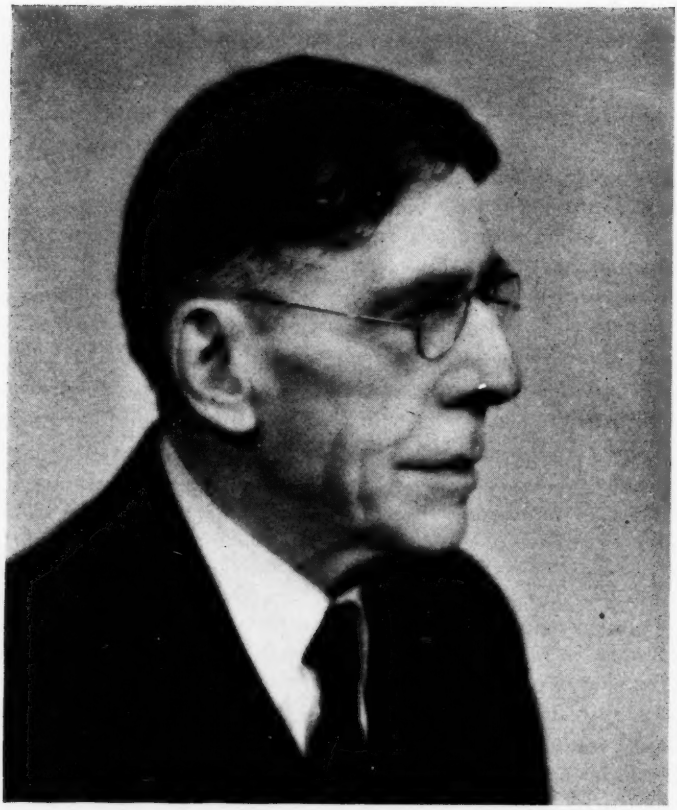
1858-1950

I met Joseph Grindon for the first time in 1908, when I was a senior medical student. He conducted a clinic—dermatologic, of course—in an ancient hospital in North St. Louis. He was a Lincolnesque figure of a man with a piercing eye and dramatic pose, and when he pointed with his stiff finger to the elementary skin lesions on a shivering, half-naked son of the soil whose adventure in venery was responsible for his presence in the clinic, that culprit winced and the medical students gazed in wonder. His dramatic description of the course and evolution of the "big pox" will never be forgotten by any of us who learned our syphilology by seeing literally dozens of cases.

His descriptions of smallpox, his story of Jenner's discovery and his dramatic presentation of the few cases of leprosy which appeared in St. Louis were classics and a delight to all who were privileged to listen.

Again I met Joe Grindon in the wards of the old City Hospital, when I was training as a fledgling intern. He was consultant to that institution, as well as to many others. Then and there did I learn for the first time that a good dermatologist was an internist with special knowledge of diseases of the skin. For Grindon was not one who looked at the skin eruption and prescribed a salve and some arsenic or other "alterative"; he examined the patient and not the skin alone and by precept and example taught us to treat the man as well as the disease. It was there that I first became aware of his linguistic ability. Into that city institution men of many nationalities were daily admitted, and few and far between were the residents who could obtain an intelligent history from those whose knowledge of English was so limited. But Grindon could converse glibly and with ease—indeed idiomatically—with the Frenchman, the Italian, the German and the Slovene. The Greek and the Spaniard, with unspoken relief, told him in their own tongue the history and course of their illnesses. I later learned that he was an expert in Latin and Greek and this knowledge was one of the reasons for his extensive and erudite studies in medical history.

Two years later, I again met Joe Grindon. In the corridors of the old Washington University Dispensary, he stopped me and wanted to



JOSEPH GRINDON SR., M.D.
1858-1950

know what I was doing. I told him I had opened an office and was waiting for patients to demand my services. "Why don't you come into our skin clinic and learn a little dermatology?" he said. I accepted his invitation; in a few months he appointed me assistant in that clinic, and my service there has been continuous ever since. Grindon was professor of dermatology then and during the three remaining years of his Washington University service was not only a teacher but also a friend and indeed a father and confessor. For all of us who worked with him could come to him with any problem, personal or professional, and be advised with wisdom, with kindliness and with compassion.

When he left Washington University to head the Department of Dermatology at St. Louis University it was a personal loss to those of us who stayed with Washington University, to participate in its phenomenal growth in the years which were to follow.

Joseph Grindon was born in St. Louis on Aug 20, 1858, the son of Arthur St. Leger and Kelis (Cherot-Dupavillon) Grindon. He was educated in the St. Louis public elementary and high schools, receiving his M.D. degree from the St. Louis Medical College in 1879 and his Ph.B. and Sc.D. degrees from St. Louis University in 1884 and 1943 respectively.

After graduation from medical school he served as intern at the St. Louis City Hospital and two years later became physician to the St. Louis Smallpox Hospital. It was during these formative years that he laid the foundation which was later to make him the outstanding local authority in the diagnosis of that epidemic disease.

From 1886 to 1895 he was lecturer on diseases of the skin at the St. Louis Medical College. In 1894 and 1895 he was professor of physiology, and from 1895 to 1899, professor of dermatology at the same institution. From 1899 to 1912 he was professor of dermatology at Washington University School of Medicine, and professor of dermatology at St. Louis University from 1912 to 1944; after 1944 he was professor emeritus.

At various times during his long career he was dermatologist to many of the private and public hospitals and clinics in St. Louis.

Dr. Grindon was a certified specialist of the American Board of Dermatology and Syphilology, a member of the St. Louis City Hospital Alumni (president, 1897), St. Louis Medical Society (president, 1899) and St. Louis Dermatological Society (president, 1914 to 1924) and a Fellow of the American Medical Association. He was also a member of the American Dermatological Association (president in 1928), Missouri State Medical Association (vice president, 1931 to 1932), Chicago Dermatological Society, Dermatological Conference of the Mississippi Valley, American Academy of Dermatology and Syphilology, Society for

Investigative Dermatology, Archaeological Institute of America, St. Louis Academy of Science, Missouri State Academy of Science, Société française de dermatologie et de syphiligraphie, Missouri Historical Society and the St. Louis Naturalists Club. He was the author of many essays and papers in medical and scientific journals and also wrote a work on "Diseases of the Skin" (1902), several chapters in the "American Text-book of Genito-Urinary Diseases, Syphilis and Diseases of the Skin" (1898) and the "Handbook of Cutaneous Therapeutics" (with Dr. W. A. Hardaway, 1907). In 1929, marking the fiftieth anniversary of his graduation in medicine, he was honored by a jubilee and reception by his former students and colleagues at both St. Louis University and Washington University.

Dr. Grindon was also a great student of medical history. He lectured on this subject to medical students for many years and contributed a number of historical articles. His thorough knowledge of ancient Greek and Latin made his historical discussion most interesting, and his ability to read and speak French, German, Italian, Greek and Spanish gave him additional advantages. He could discuss almost every scientific or cultural subject with a remarkable display of detailed knowledge, and he knew something about every branch of medicine. This interest was continued even after he was a nonagenarian, and his great sense of humor did not show any sign of waning during his declining years.

Although he was seemingly intensely interested in material affairs he did not fail to look after his spiritual welfare. Joseph Grindon was a very devout Roman Catholic. He died after a brief illness on April 1, 1950, at St. Mary's Hospital in St. Louis and was buried with a Solemn Requiem Mass from Our Lady of Lourdes Catholic Church on April 4, 1950. The church was well filled with Church dignitaries, members of religious orders, colleagues and lay friends.

Mrs. Grindon, the former Miss Lina Boisliniere, whom he married on Sept. 30, 1903, died in 1935. Surviving are his three children: Mother Pauline of the Sacred Heart Order at St. Charles, Mo.; Mrs. A. B. Murphy Jr., of San Francisco Calif., and Dr. Joseph Grindon Jr., of St. Louis.

To have lost a friend is indeed a cause for grief; that loss is personal. To have lost a great teacher is a loss for medicine, but the personality of the great teacher has a profound influence on those whom he taught, and he still lives in the hearts, the minds and the works of his pupils. Through them his thoughts, deeds and example will live on. To have lost a good man is indeed an irreparable loss to his family and to his community. He can no longer be with us to lead and to counsel us.

Let his memory be a blessing for all of us who cherish it.

RICHARD S. WEISS, M.D.

RAY HOSKINS RULISON, M.D.

1882-1950

Ray Hoskins Rulison died suddenly on Feb. 12, 1950. He was born in Jonesville, N. Y., on Sept. 30, 1882. His father was William Putnam Rulison, and his mother, Cornelia Hoskins Rulison. He received a Ph.B. degree from Syracuse University in 1903, and his medical degree from the same institution in 1907. He did postgraduate work in dermatology at the old St. Louis Hospital in 1918-1919 under Sabouraud. On his return to the United States he continued this work at the Vanderbilt Clinic, New York, from 1919 to 1920. He later became assistant clinical professor of dermatology and syphilology in the Post-Graduate Division of the School of Medicine, New York University, and also served at different times in his career as chief of the dermatologic service at Lincoln Hospital and attending dermatologist at Presbyterian Hospital, Bellevue Hospital, Cornell Clinic, New York Hospital and the New York Eye and Ear Infirmary. He was consulting dermatologist to St. Luke's Hospital, Newburgh, N. Y.; Tuxedo Memorial Hospital, Tuxedo Park, N. Y.; Goshen Hospital, Goshen, N. Y., and Elizabeth A. Horton Memorial Hospital, Middletown, N. Y.

Dr. Rulison was a member of the Founder's Group of the American Board of Dermatology and Syphilology and was certified in 1933. In the writing of dermatologic articles he always managed to present some new viewpoint on the subject.

Dr. Rulison was elected to membership in the New York Dermatological Society in December 1926 and succumbed, like all the members, to its many charms, historical, social and scientific. He manifested his interest by his attendance at all of their meetings, and he was particularly lucid in his discussions of the rare cases presented. He was fond of the usual badinage at the dinners and liked good naturedly to tease us on our boating proclivities, always describing our modest cruisers as yachts of Morgan dimensions. Because of his stay in France he was fond of the French and liked to speak the language on occasions when he was with one of us (P. E. B.).

Dr. Rulison served as a captain with the American Red Cross in World War I in Rumania and received a decoration from Ferdinand of Rumania in 1918. He continued his war service in France and became a major on Jan. 3, 1919. He returned to private practice later that year.

In 1928 he married Luenna von Eltz of New York city. Surviving him, in addition to his wife, are two sons, Michael von Eltz Rulison and William Putnam Rulison II; a brother, Dr. Foster C. Rulison, of Syracuse, N. Y., and a sister, Miss Ethel L. Rulison, of Albany, N. Y.

Dr. Rulison's death creates a great void among his close friends, including all the members of the New York Dermatological Society, of which he had recently been elected an honorary member.

PAUL E. BECHET
EUGENE F. TRAUB

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Arthur Sayer, M.D., *President*

Henry Silver, M.D., *Secretary*

Feb. 17, 1949

Lichenoid Sarcoid with Splenomegaly. Presented by DR. CHARLES WOLF.

E., a married Negro woman aged 38, born in the United States, gives no history of tuberculosis and syphilis or any other serious illness. The patient states that nodules appeared on the legs about one year ago. After an injury to the legs the lesions broke down, healed without medication and left numerous scars.

The patellar regions, thighs, buttocks and abdomen reveal numerous papules ranging in size from that of a pinhead to that of a millet seed. On the upper lip, nose and cheeks the papules are closely aggregated. Oval plaques, smooth in the center and surrounded by papules the size of a pinhead, are seen on the forehead. On the palpebral surface of the conjunctivas there are similar minute papules which an ophthalmologist considered sarcoid.

On physical examination the abdomen was seen to be distended. On palpation, the spleen was observed to be so enlarged that it filled the left side of the abdominal cavity from the free border of the ribs to a point below the umbilicus and to the right of the midline.

Roentgenographic examination failed to show enlarged hilar glands.

The Mazzini reaction to testing with a dilution of 1 : 5 was strongly positive. The icterus index was 15 (normal range, 4 to 6). Examination of the blood showed 2,800,000 red blood cells, 55 per cent hemoglobin and 4,400 white blood cells with 64 per cent polymorphonuclear cells, 32 per cent lymphocytes and 4 per cent monocytes. Tests with tuberculin in dilutions of 1 : 100,000, 1 : 10,000, 1 : 1,000 and 1 : 100 elicited negative reactions.

DISCUSSION

DR. ADOLPH ROSTENBERG: The lesions of the face impress me as lupus miliaris faciei.

DR. CHARLES R. REIN: One would expect a reversal in the albumin-globulin ratio in a case of this sort. Has determination of it been made?

DR. RUDOLF L. BAER: Has the patient been tested with BCG? Dr. Leider's work has shown that an intracutaneous test with BCG in these patients produces a sarcoid type of response similar to that seen in tests with the Kveim material, i. e., a later reaction which reaches its height after three to four weeks.

DR. MAURICE UMANSKY: That enlargement of the spleen is associated with sarcoidosis has been known since the early descriptions of the disease. In spleens removed from patients with the condition typical tubercles were found. I wonder whether this is the condition that Dr. Bloom referred to in his study as tuberculosis in the Negro (ARCH. DERMAT. & SYPH. **36**:937, 1937)?

DR. ARTHUR SAYER: A high icterus index may be associated with involvement of the liver. Blood cells are destroyed, and enlargement of the liver and spleen results.

DR. CHARLES WOLF: A common phenomenon seen in sarcoidosis is the enlargement of hilar glands, which is absent in this patient. There is no history of syphilis. On previous occasions the serologic tests gave negative reactions, but recently the reaction to the Mazzini test was positive. This is apparently a false positive reaction. The BCG test has not been performed. Another interesting feature in the case is the presence of lesions on the legs which have been interpreted as indications of possible sickle cell anemia. It should be pointed out, however, that in sickle cell anemia the ulcers do not heal as rapidly as in this case. The spleen is unusually large for that seen in sarcoidosis, although in that disease it may reach any size. There is no enlargement of the liver. Another interesting observation is sarcoid tubercles in the conjunctivas.

Localized Bullous Bromoderma. Presented by DR. NATHAN SOBEL and (by invitation) DR. LUDWIG SCHWARZSCHILD.

B. C., a white woman aged 52, registered at the New York Skin and Cancer Clinic on Aug. 13, 1948. In 1945 she had had an eruption of the legs which cleared under treatment within two months. The eruption recurred in 1947 and has persisted since. During the present year, blisters have repeatedly appeared on the legs. One of the many preparations which the patient has been taking orally contained sodium bromide.

On the anterior aspects of the lower half of the legs there are numerous bullae within erythematous patches. Although administration of bromides was stopped immediately, new bullae continued to appear fairly constantly until the middle of January 1949. Since then the number of new lesions has diminished considerably.

Serologic tests for syphilis gave negative reactions. Urinalysis showed a 3+ reaction for protein, and a negative one for sugar. Examination of the blood on Sept. 27, 1948, showed 3,800,000 red blood cells, 74 per cent hemoglobin and 5,800 white blood cells with 64 per cent neutrophils, 30 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils, 2 per cent monocytes and 2 per cent band forms. The color index was .98. On December 3 examination of the blood showed 7,600 white blood cells with 66 per cent neutrophils, 30 per cent lymphocytes, 1 per cent eosinophils, 1 per cent basophils and 2 per cent monocytes.

Examination of the fluid of a bulla on December 3 showed 50 per cent neutrophils, 43 per cent lymphocytes, 5 per cent eosinophils and 2 per cent monocytes. Examination of the urine for bromides on September 20 revealed 0.5 mg. in 1,714 cc. (twenty-four hour volume); on November 16, 19 mg. in 3,980 cc., and on Febuary 3, 1949, 6.4 mg. in 2,500 cc.

Chemical examination of the blood showed a trace of bromides. On November 6 the total protein was 8.0 per cent, with 4.8 per cent albumin and 3.2 per cent globulin and an albumin-globulin ratio of 1.5. The reactions to patch tests with potassium iodide and potassium bromide were negative on August 23 and 1+ on November 5.

A dentist reported a definite infection of a periodontal nature and no apparent abscesses. Some of the teeth appeared devitalized.

DISCUSSION

DR. LOUIS CHARGIN: The patient states that the bullous eruption appeared recently. It is difficult to accept a diagnosis of bromoderma in view of the fact that

she denies the ingestion of bromides for the past eight months. However, the patient's statement may not be reliable. It is uncommon to see bullous lesions in bromoderma. Further evidence is necessary to confirm the diagnosis.

DR. DAVID B. BALLIN: Patients receiving medication with bromides retain the bromine for a considerable period after the ingestion of the drug has been stopped, and the halogen may continue to produce the eruption long afterward.

DR. HANS H. BIBERSTEIN: I had the opportunity to see this patient at the clinic, and without knowledge of the history of ingestion of the drug I was inclined to the diagnosis of dermatitis herpetiformis. When I learned that the patient had taken a bromide preparation a few months ago I felt that this fact would not contradict the diagnosis because, like iodine, bromine may provoke a localized or generalized form of dermatitis herpetiformis.

The fact that a long period has elapsed since the patient took the drug would not militate against a diagnosis of bromoderma because bromine may be retained over an extended period. I have no information as to how the potassium iodide ointment for the test was prepared. When it is not correctly prepared one may get a negative reaction even in cases in which a positive reaction is expected and can be elicited.

DR. NATHAN SOBEL: Originally the patient presented many bullae on the legs. Prompted by Andrews' work (*New York State J. Med.* **48**:2029, 1948) a search for foci of infection was made but was unsuccessful.

DR. LUDWIG SCHWARZSCHILD (by invitation): The case is of interest because the patient presents only bullae and none of the other types of lesions which one is accustomed to see in bromoderma. After the administration of salt tablets the increase of bromine in the urine was considerable, from 0.5 to 19 mg.; recently it has decreased to 6.5 mg. in a twenty-four hour specimen. It is also possible that the patient may have ingested bromine in the form of foods, as many vegetables and foods are known to contain small amounts of bromine.

Basal Cell Epithelioma of the Scalp Treated with Chemosurgery (Mohs). Presented by DR. HENRY SILVER and DR. MAX BERKOVSKY.

Infiltrating Anaplastic Epithelioma Arising from a Basal Cell Epithelioma: Cured by Chemosurgery. Presented by DR. WILBERT SACHS and DR. PERRY M. SACHS.

J. W., a man aged 41, had an ulcerating lesion which was first noticed in 1946 and treated with ointments. On April 21, 1947, the patient presented on the anterior parietal area a deep, ulcerating, bleeding and crust-covered tumor the size of a silver dollar. This ulcerating mass reached deep down into the galea.

Microscopic examination showed infiltrating anaplastic epithelioma arising from a basal cell epithelioma. After the type of lesion had been established, chemosurgery was resorted to. The ulcerating mass healed completely, leaving a smooth scar in that area.

DISCUSSION OF CASES OF EPITHELIOMA

DR. RUDOLF L. BAER: What is the advantage of the Mohs treatment over the usual procedures employed by dermatologists? Does a small defect result from that form of therapy? Did Dr. Sachs observe any strands of cells growing outside of the clinically suspect area?

DR. LOUIS CHARGIN: The results are splendid, but I do not see any particular advantage in using the Mohs method of therapy once the diagnosis has been

established by biopsy. It may perhaps have been useful in dealing with the anaplastic lesion. In basal cell epithelioma one obtains more rapid and equally satisfactory results by the well known methods employed. The Mohs method is more complex and difficult and may have its application in the rare case.

DR. CHARLES WOLF: Many basal and squamous cell epitheliomas are apparently cured by routine methods. Dr. Sachs is of the opinion that there are still carcinomatous cells left in many cases. How can he determine whether he has eradicated every malignant cell in the area affected, and what criteria does he employ to judge whether he has effected a permanent cure?

DR. CHARLES R. REIN: How large were the lesions as compared to the scars now present?

DR. HARRY B. FEILER: A patient under my observation who presented a lesion on the scalp about the size of a dime was twice treated by desiccation while serving in the United States Army. Biopsy of the recurrent lesion showed anaplastic epithelioma. No biopsy had been performed previously. Dr. Sachs treated the patient by the Mohs method, and there had been no recurrence in a year.

DR. WILFERT SACHS: I am of the opinion that radiation therapy is of little or no value in the treatment of anaplastic epitheliomas; in fact, it may be detrimental. These epitheliomas do have strands running in all directions away from the site of the lesion. Therefore, since the lesion extended almost to the bone in the case cited by Dr. Feiler, I employed the Mohs treatment. In Silver and Berkovsky's case I used the Mohs method because I was told that there had been some attempt at removal of the lesion, with recurrence. By the Mohs method I found that the lesion undermined the scalp. How do I know that there is cure in these cases? That is the entire purpose of the Mohs method. Each section is examined under the microscope and treated until there are no more malignant cells left. Usually the scars are about one-third the size of or smaller than the original lesions.

Squamous Cell Epithelioma Following Radiodermatitis and Basal Cell Epithelioma in the Same Patient. Presented by Dr. WILLIAM M. SISKIND.

M. K., aged 57, is the mother of 5 children, all of whom are living and well. There is no history of tuberculosis in the family. However, about twenty-two years ago the patient had tuberculosis of the left side of the neck. She was treated at a local hospital with roentgen rays, but the amount given could not be ascertained. Seven years later there developed a radiodermatitis on the treated side. Four months ago she noticed a small growth on the left side of the neck, which soon became crusted and ulcerated.

At present the left side of the neck shows the characteristic changes of radiodermatitis. At the upper pole of the involved area there is an ulcerated lesion. On the right ala nasi there is a bloody, crusted lesion, and on the right cheek, a small nodular lesion with a pearly border. This lesion is of two years' duration.

Histologic examination of the ulcerated lesion of the left side of the neck showed squamous cell carcinoma. Permission for a biopsy of the lesion on the nose was refused.

DISCUSSION

DR. FRANK E. CROSS: This patient has two different types of cancer of the skin, and I believe there is no relation between the two lesions.

DR. CHARLES WOLF: One should not lightly state that one epitheliomatous lesion has nothing to do with the other. There are records of basal cell epitheliomas

having metastasized. If a patient acquires an epithelioma remotely from the original site several possibilities as to the origin should be considered. Would Dr. Sachs employ the Mohs treatment in this case?

DR. WILBERT SACHS: It is not uncommon to find basal cell and prickle cell epitheliomas in the same patient. I cannot conceive how a basal cell tumor can metastasize as a squamous cell one or the reverse. I certainly would use the Mohs method on the prickle cell lesion. I have seen epitheliomas on the basis of radiodermatitis heal much better with Mohs's method than with any other treatment.

Scleredema Adultorum (Buschke) Extending Down to the Hips. Presented by DR. JULIUS H. POLLOCK.

Alopecia Areata Totalis: Three Cases. Presented by DR. JOHN GARB.

Arthur Sayer, M.D., *President*

Henry Silver, M.D., *Secretary*

March 17, 1949

Mycotic Eczema Due to Epidermophyton Inguinale. Leukemia Cutis? Presented by DR. JOHN GARB and DR. ANDREW G. FRANKS.

C. N., a woman aged 24, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 8, 1949, complaining of a cutaneous eruption of six months' duration. She comes from the West Indies and has been residing in this country for the past year and a half. In 1939 she had furuncles and abscesses.

On the trunk and extremities there are well defined large patches with exaggerated markings of the skin. They are moderately infiltrated and are covered with fine, adherent powder-like scales. Almost the entire body is covered with these diffuse sheets except for the lower two thirds of the forearms and hands, the central portion of the face, the scalp and the upper part of the back. The patches on the right side of the neck are considerably thicker and rougher and more tender and painful than those in the other areas. The dorsal surfaces of the feet are affected but not the soles. Besides these large patches there are also numerous match head–sized to split pea–sized round isolated and grouped papules.

The Wassermann tests of the blood, repeated twice, gave weakly positive reactions. The hemogram showed 3,600,000 erythrocytes and 10.7 Gm. of hemoglobin per hundred cubic centimeters of blood (74 per cent). The color index was 1.02. The leukocyte count was 11,500 with a differential count of 35 polymorphonuclear cells, 64 per cent lymphocytes and 1 per cent eosinophils. There were many toxic and atypical lymphocytes.

A histologic section of a lesion on the right side of the neck was interpreted as superficial dermatitis. The epidermis was slightly acanthotic and showed a spotty parakeratosis. The upper portion of the cutis was edematous and the blood vessels dilated. There was diffuse and focal nonspecific inflammatory reaction throughout the upper part of the cutis and the midcutis.

Scrapings of three patches were positive for tinea. Culture of the scrapings of the lesion on the neck showed the characteristic grayish olive drab color, with a velvety surface and irregular folds and grooves, characteristic of Epidermophyton inguinale.

DISCUSSION

DR. EMANUEL MUSKATBLIT: Mycotic diseases of the skin are usually limited in extent. Cases with widely distributed lesions are rare. The clinical manifestations in this case seem to be torpid; there is no inflammatory response and no erythema, and the skin is dry, scaly and lichenified. The papular hyperkeratotic lesions were present before the mycosis developed. However, the lichenified scaly skin is of mycotic character. An interesting feature of this case is that the nails are not affected, in spite of the wide distribution of cutaneous lesions. Still another unusual feature is the observation that the fungus E. inguinale is the cause of the disease. This fungus usually causes limited lesions such as those of tinea cruris, tinea axillaris and dermatophytosis of the feet. Generalized cases in this country are due mostly to Trichophyton purpureum. The culture is typical in its configuration and color. I believe that this patient will be a difficult one to treat because of the wide generalization of the lesions and the lack of inflammatory response. Moreover, the environment of this patient is probably full of infectious material, and reinfection can easily occur from hidden foci.

DR. ANDREW G. FRANKS: I agree with Dr. Muskatblit. I took the opportunity of asking several mycologists in the city as to the frequency with which they have seen such generalized cases. One stated that in seventeen years he has seen 2 cases, and another saw 1 in four years. In China such cases are common but differ clinically; they present vesicular lesions with considerable inflammatory reaction. We may be dealing with multiple fungi; the cultures should settle this question.

DR. JOHN GARB: The nodules in the groin are probably similar to those on the trunk but look different because of moisture and friction in that location. The patient might have had generalized eczema, after which the E. inguinale, being a secondary invader, developed rapidly because of the favorable soil. The blood picture, which shows a high lymphocyte count with many atypical lymphocytes, suggests that the papular growths may be of different origin than the patches of tinea and may in the end prove to be lymphoblastoma.

ADDITIONAL NOTE.—On April 11, 1949, the patient was transferred to Bellevue Hospital. She was going rapidly downhill and died on May 15, 1949. The final diagnosis was subacute lymphatic leukemia and leukemia cutis.

Steatocystoma Multiplex. Presented by DR. NATHAN SOBEL.

F. T., a white woman aged 27, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 19, 1949, presenting lesions of one year's duration. On the neck, right forearm, back of the chest and abdomen there are many elevated, smooth, moderately firm papules and nodules with a pronounced yellow tinge, varying in size from that of a pinhead to that of a large pea.

The histologic diagnosis submitted by Dr. C. Miller and P. Sachs was steatocystoma multiplex.

DISCUSSION

DR. FRANK E. CROSS: These cases are not common. They are not the ordinary sebaceous cysts. Steatocytoma multiplex is an entity. Lisi expressed the opinion that the condition is a cystic sebaceous nevus. One almost never sees lesions on the scalp. The cysts occur on the upper anterior portion of the trunk, back, arms, buttocks and thighs. There may be from 500 to 2,000 or more of these cystic

lesions. Sooner or later some of them become secondarily infected, as do sebaceous cysts, and break down and form scars.

The general impression is that there is no cure for this condtion. About five years ago I had under my care a patient who had about 700 of these cysts in the usual locations. I treated him as follows: I injected into about six of these cysts procaine hydrochloride (novocain®) at one session, then punctured each cyst with a cataract knife, expressed the contents and then thoroughly desiccated the inner surface of each lesion in a rotary motion through the punctured area. I repeated this session about every five days for about eighteen months. The result was good. While this method is simple, I never saw it reported in the treatment of steatocytoma multiplex (Pringle).

DR. WILBERT SACHS: May I point out to Dr. Cross that some of these patients do have lesions on the scalp? There is a picture of lesions in the scalp in a paper that I published (ARCH. DERMAT. & SYPH. **38**:877-880, 1938).

DR. MAX JESSNER: Some years ago I saw such a case in Breslau, and at that time the lesions were limited to the axillas. Recently I saw this same case in New York city with Dr. Sulzberger, and at that time the patient showed extensive lesions, disseminated over a large part of the body. It is interesting to note that her son now has the same condition.

Neurodermatitis Circumscripta of the Hand Successfully Treated with Thorium X. Presented by DR. NATHAN SOBEL and (by invitation) DR. LUDWIG ISAAK.

A. F., a man aged 67, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 6, 1948. The entire dorsal surface of the left hand showed numerous light brown papular lesions, both discrete and occurring in plaques. The duration was one year. The histologic diagnosis submitted by Dr. M. Jessner was probable neurodermatitis.

Treatment with ointments containing tar failed to influence the eruption. The patient then was given an ointment with 2,000 electrostatic units of thorium X per cubic centimeter. This was applied for forty-eight hours each time on four different visits: July 23 and 28, and Aug. 4 and 11, 1948. Considerable improvement was noticeable after the first application. A slight radiation erythema (alpha radiation effect) appeared after the third and fourth applications but cleared within one week. From August 18 to September 22 pronounced pigmentation was present. On October 22 the lesion had healed. There has been no recurrence.

DISCUSSION

DR. MAX JESSNER: I think that the dose of thorium X given in this case and the short intervals may discredit this form of treatment in this country. Thorium X therapy dates back thirty-seven years. It was by pure chance that the action of thorium X on the skin was detected. In a case of leukemia cutis in which it was given subcutaneously, a berlock dermatitis–like inflammation developed the following day at the site of the injection. It was thought that a drop of the solution must have run over the skin and caused the inflammatory reaction. This disappeared in about one and a half weeks and was followed by pigmentation. Thorium X solutions were then tried in the form of wet dressings and incorporated in anhydrous ointment bases for various diseases of the skin, and finally a treatment schedule was worked out. Since histologic changes in the skin are observed up to six weeks after a single application, one should not give

thorium X at less than six week intervals. At such intervals I have never seen any damage resulting from thorium X therapy. It was the only treatment my associates and I employed for nevus flammeus. I do not know of 1 case of nevus flammeus in which the lesion did not become much lighter, and many lesions disappeared entirely. Of course, the treatment extends over a considerable period. Each patient requires about seven to ten treatments, and, with the intervals of six to ten weeks between them, treatment may often require about two years. In Europe thorium X was also used in the treatment of many diseases, such as psoriasis, discoid lupus erythematosus, morphea and neurodermatitis. It is a helpful remedy, but one ought not be tempted to give it in too high a dose and at too short intervals.

DR. LUDWIG ISAAK (by invitation): I am grateful to Dr. Jessner for his remarks. I gave the treatment based on the experience I had had with radon ointment, which I used about eight years ago and which gives about the same radiation as does thorium X (ARCH. DERMAT. & SYPH. **45**:560, 1942). Thorium X is practically an alpha radiator, giving off 92 per cent of alpha rays, 4 per cent of beta rays and 4 per cent of gamma radiation. The alpha radiation is absorbed in 0.1 mm. of tissue. Therefore, it is most improbable that the capillary layer of the skin can be damaged by that kind of radiation. Certainly, if one gave larger doses, and if more beta and gamma radiation were effective, damage would occur. Whenever I applied thorium X ointment in weekly intervals for forty-eight hours, after a certain number of applications—sometimes after two, sometimes after three or four—erythema appeared and the treatment had to be stopped. I got really good treatment effects only when there was noticed an erythema, which usually disappeared within a week, followed by pigmentation, which lasted for one month. I do not think that any sequelae from that kind of treatment can be expected. At least so far none have been seen from radon ointment. I discussed the amount of radiation given in that case with our physicist, Dr. Mutscheller. One cannot compare the soft ray radiation and its "erythema dose" with doses of roentgen rays or radium rays. But mathematically 2,000 electrostatic units of thorium X applied for forty-eight hours are equal to about 0.6 erythema dose of radium (1 microcurie equals 2.75 electrostatic units). That would mean, if the radiation had come from a point, that about two and a half erythema doses would have been given within four weeks. Moreover, those 2,000 electrostatic units are incorporated each in 1 cc. of ointment, each cubic centimeter being enough to irradiate 100 square centimeters, or 16 square inches. In reality, therefore, each centimeter or square inch receives only a small fraction of the total radiation. When one compares this quantity of radiation with the quantity of roentgen rays usually given in such cases, one finds that it certainly is not greater. Had I given smaller amounts of radiation, I think I would not have been able to cure the condition in so short a time. All other conditions with hypertrophic lesions, such as lichen planus hypertrophicus and lichenified eczema, which usually do not respond well to roentgen therapy, clear up under treatment with thorium X.

Kaposi's Sarcoma in a Woman. Presented by DR. ADOLPH ROSTENBERG and DR. WILLIAM M. SISKIND.

Sarcoidosis of the Skin, Bones and Lungs: Improvement Coincident with Use of BCG Vaccine. Presented by DR. MORRIS LEIDER.

Lichenoid Sarcoid. Presented by DR. DAVID B. BALLIN.

Disseminated Lupus Erythematosus Following Pregnancy. Latent Syphilis? Presented by DR. ALEXANDER A. FISHER.

Papulonecrotic Tuberculid and Erythema Induratum? (Halogen Sensitivity?). Presented by Dr. William M. Siskind.

Chronic Actinic Dermatitis with Keratoses. Presented by Dr. Frank E. Cross.

Necrobiosis Lipoidica Diabeticorum. Presented by Dr. Martin V. Boardman.

BROOKLYN DERMATOLOGICAL SOCIETY

E. Almore Gauvain, M.D., *President*

Seymour H. Silvers, M.D., *Secretary*

Feb. 21, 1949

Chronic Lupus Erythematosus Successfully Treated with Vitamin E. Presented by Dr. Seymour H. Silvers.

H. L., aged 31, when first seen by me four weeks ago showed an extensive eruption of lupus erythematosus of the face, nose and forehead. It had never before been treated. The lesions involved approximately one half of the skin of the face. The patient requested treatment because he had been refused employment because of his disfigurement. He received daily injections of 100 mg. of alpha tocopherol intramuscularly, with a total dose of twenty-seven injections, and 150 mg. of alpha tocopherol given daily by mouth.

Examination shows decided improvement.

Further Observation.—The lesions continued to improve under oral therapy with 300 mg. of alpha tocopherol given daily.

DISCUSSION

Dr. Seymour H. Silvers: This man was treated for only twenty-seven days. This is the twenty-seventh day, and he definitely shows improvement. I have 2 more patients whom I am treating with alpha tocopherol. They, too, show as good improvement as one would expect to see after bismuth or gold therapy.

Dr. H. L. Feigenbaum: One of my associates at the clinic has treated about 6 patients with chronic discoid lupus erythematosus with vitamin E. He has been able to give them vitamin E only by mouth and in doses of 150 mg. per day. He claims he has observed 30 to 40 per cent improvement within the last six weeks. These were cases in which the condition had previously responded to gold and to bismuth therapy but had recurred.

Erythema Multiforme Bullosum (Stevens-Johnson Syndrome) Treated with Aureomycin. Presented by Dr. Aruthr M. Persky.

R. M., a Negro girl, aged 11, is presented because of the response of her condition to aureomycin therapy.

Two days before admission, the patient acquired a sore throat and took a few doses of an ammonium chloride cough mixture. The following day the temperature began to rise and a generalized bullous eruption resulted. The patient was admitted with a temperature of 104 F., a generalized bullous, erythematous eruption, ulceration and hemorrhages of the mouth. She was unable to swallow. Fluids were given intravenously, and diphenhydramine (benadryl®), penicillin every three hours and sedation were administered. No change occurred after two days, and the leukocyte count, which had been 6,000 on admission, dropped to 4,000 per cubic centimeter. Blood and plasma were then administered daily, and strepto-

mycin intravenously, without improvement. At this point treatment with aureomycin was started; 750 mg. was administered every four hours until 14,000 mg. was received in a three day period. With the initiation of aureomycin therapy, the patient's condition began to improve, the temperature dropping to normal slowly and the bullae becoming reabsorbed. The conjunctivitis which had been present on admission began to clear, and the ulcerations of the mouth healed so that oral feedings were possible. As recovery started, an obstructive jaundice developed. The liver was never enlarged nor tender, but bile was found in the urine and the icterus index varied between 50 to 70. The skin has healed uneventfully except for pigmentation and some lichenoid infiltration over the scapular region.

DISCUSSION

DR. ABRAHAM WALZER: Stevens-Johnson disease is just one type of erythema multiforme. It is not an entity.

Idiopathic Multiple Hemorrhagic Sarcoma (Kaposi). Presented by DR. ROBERT L. REIN.

Darier-Roussy Sarcoid. Presented by DR. M. M. ESTRIN.

A Case for Diagnosis: Poikiloderma? Atrophic Lichen Planus? Lichen Sclerosis et Atrophicus? Presented by DR. SEYMOUR H. SILVERS.

A Case for Diagnosis: Late Syphilis of the Skin? Drug Eruption? Presented by DR. M. J. CANTOR.

Lichen Planus Hypertrophicus. Presented by DR. ARTHUR M. PERSKY.

Dermatomyositis Associated with Avitaminosis in a Boy Aged 10. Presented by DR. A. FRIEDMAN (by invitation).

A Case for Diagnosis: Generalized Herpes Zoster? Presented by DR. A. FRIEDMAN (by invitation).

Generalized Argyria. Presented by DR. M. J. CANTOR.

Keratosis Blennorrhagica. Presented by DR. A. FRIEDMAN (by invitation).

CHICAGO DERMATOLOGICAL SOCIETY

Carl W. Laymon, M.D., *President*

James R. Webster, M.D., *Secretary*

March 16, 1949

Sickle Cell Anemia with Ulceration of the Lower Extremities in a Negro Girl Aged 19. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. ROBERT H. HARRIS.

Sickle Cell Anemia with Three Year Old Ulcer of the Lower Extremities in a Negro Aged 39. Presented by DR. JAMES H. MITCHELL and (by invitation) DR. ROBERT H. HARRIS.

DISCUSSION OF CASES OF SICKLE CELL ANEMIA

DR. THEODORE CORNBLEET: I thought these cases were interesting. The best agent we have found thus far in treatment of sickle cell anemia ulcers has been red blood cell paste or even blood muck from the blood bank applied to the lesions themselves. The man is 39 years old, and that is fairly old for a person with sickle cell anemia. By and large we see this disease in younger people. The changes seen in the skull in children with the disorder are similar to those seen in erythroblastosis. The specific anemia disease as such is uncommon in

the large group showing the sickling trait, appearing in only 1 out of 40. The girl's case was somewhat unusual in that there were lesions on both legs and feet.

DR. FRANCIS W. LYNCH, St. Paul, Minn.: I should like to inquire what happens to these lesions with the passage of time. Many of us have little or no experience with this disorder.

DR. THEODORE CORNBLEET: The patients that we have been able to follow for extended periods have had relapses with reappearances of the ulcers at the original sites. Anemia can and does appear with dramatic suddenness, often dishearteningly, after the blood has been built up slowly. It is said that the ulcers can be explained on the basis of embolism. It is difficult for me to accept this hypothesis for a number of reasons, but I have no better one. There may be widespread visceral changes which are apt to appear with crises of fever and constitutional changes.

DR. ROBERT H. HARRIS (by invitation): The factor that leads to actual production of sickle cells is diminution in the oxygen tension. The process is reversible. Both patients have lesions of the heart, and anoxemia due to that condition could cause sickle cell formation.

Regarding the bone lesions, there is an article in the *Journal of Radiology* for August 1948 in which such changes are described. The treatment prescribed by Dr. Mitchell for the ulcers was the use of a cod liver oil and white wax ointment. It seems to be successful because with bed rest the man is having very rapid healing of the ulcer.

Linear Scleroderma en Coup de Sabre and Morphea of the Back. Presented by DR. LOUIS RUBIN (by invitation).

DISCUSSION

DR. LOUIS RUBIN (by invitation): This is the second case we have had at the University of Chicago of linear scleroderma of the scalp with morphea on the trunk, which observation would seem to add further evidence that these lesions are manifestations of the same disease. We are somewhat concerned about this woman from a prognostic standpoint. While she has been receiving treatment she has acquired some depigmentation on the right ala nasi, and we wonder whether the condition is going to develop into progressive facial hemiatrophy.

A Case for Diagnosis. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. D. COHEN and DR. S. BARSKY.

V. A., is a 7 year old Negro girl who has had a noninflammatory, intermittent papular eruption of the face for about four years.

The eruption was first noted about four years ago. The lesions clear up completely each fall but recur in the early spring. Associated with the eruption on each occasion has been "pink eye."

The patient is in good general health and has not recently been ill.

On physical examination there is seen a noninflammatory, uniform, pinhead–sized, papulocystic eruption involving the forehead, bridge of the nose, nasolabial area and cheeks. Pricking the lesions with a hypodermic needle reveals no fluid or cheesy contents. A mild bilateral conjunctivitis is noted. Mild scaling is present on the scalp. The heart, lungs and results of a general physical examination were normal.

Laboratory examination revealed the following data: urine, albumin and glucose not observed on microscopic examination; serologic picture, normal; hemoglobin, 90 per cent; white blood cell count, 6,500, and roentgenogram of the chest, normal. Biopsy of one of the lesions on the face was reported as revealing acute dermatitis.

DISCUSSION

DR. M. R. CARO: I should merely like to make an explanation of the histologic diagnosis. The section I examined showed a considerable amount of edema in the epidermis. Apparently the section was not cut deeply enough in the specimen to include the diseased tissue.

DR. THEODORE CORNBLEET: It might be thought that this is an eruption of miliaria, but the lesions are solid. There is no exudation or collapse on puncture. The face has been affected in this manner, apparently without obvious change, for a considerable time. The lesions were shown on histologic grounds to be lichen urticatus.

NOTE.—Later sections cut from another part of the specimen showed histologic findings diagnostic of lichen nitidus.

Adenoma Sebaceum and Cutaneous Horn. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. D. COHEN and DR. D. MUSGRAVE.

DISCUSSION

DR. THEODORE CORNBLEET: I thought it was of added interest that the lesions were almost entirely unilateral.

A Case for Diagnosis: Chapped Skin in a Woman with Diabetes. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. D. MUSGRAVE.

DISCUSSION

DR. STEPHEN ROTHMAN: This patient has mild ichthyosis vulgaris with characteristic sparing of the large folds.

The pathogenesis of diabetic pruritus is poorly understood. It is a notorious fact that pruritus in diabetes is not in proportion to the severity of the disease. In mild cases, itching may be intolerable. In severe cases, particularly in juvenile diabetes, pruritus is not often encountered. On the other hand, the skin in diabetes is dry, and it seems that xerosis and diabetes have to be combined in order that pruritus may be elicited. In many cases, relief is obtained by simple greasing of the skin without control of the diabetes. The deficiency of the oily film on the skin surface in diabetic pruritus deserves systematic study.

Lupus Vulgaris of Forty Years' Duration with Mitotic Process in Lupo. Presented by DR. ROBERT H. SNAPP (by invitation).

DISCUSSION

DR. STEPHEN ROTHMAN: This patient is unable to state whether or not she had roentgen therapy when she was a child.

In the twenties, when unduly high total doses of roentgen rays were given for lupus in Germany, I was thoroughly convinced that practically all lupus carcinomas are roentgen ray carcinomas. All those tumors arose in areas which were grossly damaged by roentgen rays. My experience in this country taught me to believe that lupus vulgaris actually can be regarded as a precancerous

state because I saw here 3 cases with spontaneous carcinoma in lupo with no history of roentgen ray treatment and no signs of actinodermatitis.

Concerning the development of cancer in lesions of chronic discoid lupus erythematosus, I refer to the review article of Charles Ryan in the *British Medical Journal* (**2**:334 [Aug. 30] 1947). He found in the literature over 100 cases of carcinoma complicating lupus erythematosus in which no roentgen rays

Lupus vulgaris of forty years' duration with carcinoma in lupo.

or radium had been given. He concluded that the inflammatory changes which precede the atrophy in lupus erythematosus may lead unaided to cancer formation.

A Case for Diagnosis. Presented by DR. F. J. KENDRICK, Gary, Ind. (by invitation) and DR. BERNARD YAFFE (by invitation).

Mrs. C. R., a 32 year old white woman, has had some twenty cutaneous tumors in the past six or seven years, treated by us and others. Most of these tumors

have appeared on the face, including the lips and border of the nasal septum, and on the extremities.

Usually, one of these tumors appears within a week or so and grows to dime size in a month. None have been allowed to grow larger. The individual lesions are generally firm, rather pearly bordered and verrucous or ulcerated centrally.

Many biopsy specimens have been taken and reported as warts, basal and squamous cell epitheliomas and, more recently, hornified epithelial cysts. We have not seen all of them.

Roentgen irradiation, cautery and surgical measures have each been used effectively on individual lesions.

The most recent lesions were one on the lower lip and one on the right leg. These have both been considered hornified epithelial cystic lesions of some sort.

The last-mentioned biopsy specimens and several others are shown.

DISCUSSION

DR. S. W. BECKER: This case reminds me of that of a man Dr. Stenhouse and I presented here Nov. 19, 1941 (ARCH. DERMAT. & SYPH. **45**:999 [May] 1942). The patient had multiple tumors of the skin which microscopically showed some of the architecture of squamous cell carcinoma, but according to the history at least some of the tumors had healed spontaneously. Smith reported 3 similar cases (*Brit. J. Dermat.* **60**:315-318 [Oct.] 1948). The microscopic sections from this patient show one of the characteristics of carcinoma—namely, penetration—but little if any anaplasia of the surface epithelium or parakeratotic change such as is seen in keratosis. Some of the penetrating epithelium contains pearls or pseudopearls. I think the only way to be sure of the diagnosis would be to let one of these tumors grow, which is not recommended as a therapeutic procedure. The lesions may be classified as group 1 squamous cell epithelioma, practically a benign tumor. I belive that the patient will probably have others.

DR. L. F. WEBER: I thought the lesions were self induced.

DR. M. R. CARO: That is the impression I had. I could not quite convince myself that the history was suggestive of neurotic excoriations, but the histologic picture could be consistent with the changes seen in neurotic excoriations.

Ulcerated Tertiary Syphilis of the Leg. Presented by DR. D. OMENS and DR. H. RATTNER and (by invitation) DR. H. OMENS and DR. D. MUSGRAVE.

Tertiary Syphilis: Serpiginous Plaques, Generalized but Asymmetric. Presented by DR. M. EBERT and (by invitation) DR. H. OMENS and DR. S. BARSKY.

Chronic Discoid Lupus Erythematosus of the Scalp and Face. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. S. BARSKY.

A Case for Diagnosis: Lupus Erythematosus of the Scalp? Presented by DR. F. J. KENDRICK, Gary, Ind. (by invitation) and DR. BERNARD YAFFÉ.

Chronic Lymphatic Leukemia. Nodules on Legs. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. D. MUSGRAVE.

Giant Follicular Lymphadenopathy (Brill-Symmers Disease) with Cutaneous Tumors. Presented by DR. LOUIS RUBIN (by invitation).

A Case for Diagnosis: Spiegler-Fendt Sarcoid (?) at Site of Performance of Dick Test. Presented by DR. ALBERT H. SLEPYAN.

Early Xanthoma Tuberosum Multiplex of the Skin. Presented (by invitation) by DR. JAMES E. ENGELER, Lafayette, Ind.

Pityriasis Rubra Pilaris in a 5 Year Old Boy. Presented by DR. JAMES H. MITCHELL and DR. F. W. HETREED (by invitation).

Pityriasis Rubra Pilaris of Two Years' Duration in a 7 Year Old Boy. Presented by DR. JAMES H. MITCHELL and DR. F. W. HETREED (by invitation).

A Case for Diagnosis: Atrophic Scleroderma? Necrobiosis Lipoidica Diabeticorum? Presented by DR. CLEVELAND J. WHITE.

A Case for Diagnosis: Ulcer of the Tongue in a Ten Month Old Infant. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. D. MUSGRAVE.

Papular Sarcoidosis of the Face and Legs. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. SCHORR and DR. D. MUSGRAVE.

Peculiar Longitudinal Striations of the Scalp in a Man with Erythema Multiforme. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. SCHORR and DR. S. BARSKY.

Generalized Lichen Planus. Presented by DR. J. WEBSTER and DR. S. BLUEFARB and (by invitation) DR. S. BARSKY.

Folliculitis Decalvans. Presented by DR. H. RATTNER and (by invitation) DR. H. RODIN and DR. S. BARSKY.

A Case for Diagnosis: Congenital Defect of Nails and Heart? Presented by DR. JAMES R. WEBSTER and (by invitation) DR. FRANCIS HETREED and DR. ALFRED B. FALK.

Lepromatous Leprosy in a Mexican. Presented by DR. J. RODRIQUEZ, DR. M. ROBIN, and DR. S. WEINSTEIN, from the Chicago Intensive Treatment Center, under the direction of Dr. Herman N. Bundesen, president, Chicago Board of Health, and Dr. Frederick Plotke, Venereal Disease Control officer (by invitation).

CLEVELAND DERMATOLOGICAL SOCIETY

Earl W. Netherton, M.D., *President*

George H. Curtis, M.D., *Secretary*

Gerard A. DeOreo, M.D., *Reporter*

Feb. 24, 1949

Keratoderma Palmaris and Plantaris? Verruca Vulgaris? Presented by DR. H. H. JOHNSON and DR. C. G. ZAGIOB (by invitation), St. Luke's Hospital.

Keratosis Palmaris et Plantaris (Arsenical); Epitheliomatosis. Presented by DR. B. PERSKY and DR. N. R. KRUPKIN (by invitation).

A Case for Diagnosis: Prurigo Ferox of Hebra? Lymphoblastoma? in a Thirty-Two Year Old Man. Presented by DR. I. L. SCHONBERG and DR. M. HANTMAN (by invitation).

Lupus Erythematosus of the Eyelids. Presented by DR. I. L. SCHONBERG.

Dermatitis Herpetiformis Prominent in Flexural Areas. Presented by DR. I. L. SCHONBERG.

Sarcoidosis of the Skin. Presented by DR. H. H. JOHNSON and DR. C. G. ZAGIOB (by invitation), St. Luke's Hospital .

A Case for Diagnosis: Seborrheic Dermatitis? Lupus Erythematosus of the Scalp? Presented by DR. BENJAMIN LEVINE.

A Case for Diagnosis: Leukoplakia? Lichen Sclerosus et Atrophicus? of the Glans Penis. Presented by DR. B. LEVINE.

Earl W. Netherton, M.D., *President*

George H. Curtis, M.D., *Secretary*

Gerard A. DeOreo, M.D., *Reporter*

March 24, 1949

Subacute Disseminated Lupus Erythematosus. Presented by DR. E. W. NETHERTON.

Acute Disseminated Lupus Erythematosus. Presented by DR. JOHN R. HASERICK.

Mrs. R. V., aged 26, was admitted to the Cleveland Clinic Hospital on Jan. 28, 1949. In October 1948 the patient acquired a temperature of 103 F., with constant and severe pain in the left upper portion of the abdomen. She was hospitalized because of a "kidney infection" and "ovarian trouble." She received penicillin and streptomycin therapy but acquired an eruption. She remained in

the hospital for three weeks. At home, she continued to have a low grade fever and had intermittent distress in the knees, ankles and elbows. In November 1948 her local physician ordered her to bed for four weeks because of a cardiac murmur. Later she was told that this murmur had disappeared. In December 1948 she had severe pain in the left side of the chest, associated with fever and coughing, which lasted about one week. In January 1949 anorexia developed, in association with bloating and abdominal distress, with some swelling of the abdomen. One week prior to admission swelling of the face and ankles developed.

The history revealed that four years ago the patient had had swollen joints of the knees and fingers following a pregnancy. A diagnosis of rheumatic fever had been made. She had recovered well from that attack but had had a relapse one year later. This attack had consisted of severe joint pains and low grade fever, and she was treated with salicylates, with some relief. After a short remission, she again had swollen and painful joints. The arthritic pains were mostly in the shoulders, neck, feet, knees, hips and elbows.

Physical examination in January 1949 revealed a temperature of 99.6 F. and a pulse rate of 112 per minute. The blood pressure was 194 systolic and 140 diastolic. A slight speckled, erythematous rash was noted over the neck and upper portion of the chest on admission, but this disappeared after a few days of hospitalization. Examination of the chest and lungs revealed normal expansion. There was dulness over the lower lobe of the left lung, posteriorly, with diminished tactile fremitus and breath sounds. A gallop rhythm with a split first sound was heard over the apex. The liver was not palpable. There was moderate tenderness in the left upper quadrant, and the abdomen was somewhat distended. A definite fluid wave was present, associated with shifting dulness. There was no swelling or redness of any of the joints. A 3 + pitting edema of the sacrum and ankles was noted.

The routine urinalysis on January 29 revealed a 4 + reaction for albumin, a specific gravity of 1.015 and a p_H of 5.5. Numerous red blood cells were present, as well as 5 to 10 white blood cells per high power field. The blood urea ranged from 57 mg. to 114 mg. per hundred cubic centimeters one week after admission. The Wassermann and Kahn reactions were negative. The hemoglobin was 10.5 Gm. per hundred cubic centimeters. The erythrocytes count was 3,960,000. The leukocyte count was 3,350, with 77 per cent neutrophils. An examination of bone marrow revealed numerous lupus erythematosus cells.

The patient acquired severe ulcerations of the mouth and lips. Her course has been one of gradual improvement, coincident with a blood transfusion and the intravenous administration of aureomycin.

Lupus Erythematosus with Involvement of Lower Eyelids and Buccal Mucous Membrane. Presented by DR. CLYDE L. CUMMER.

DISCUSSION OF CASES OF LUPUS ERYTHEMATOSUS

DR. H. J. PARKHURST: I felt that there was considerable likelihood that the first case would develop to be one of acute disseminated lupus erythematosus because of the fact that the recorded white blood cell count had been 2,100. I felt that the second case was already one, since the lupus erythematosus cells had been found in the bone marrow, and that the last case was one of the discoid type. I was very much interested in the lesions in the buccal mucous membrane and the conjunctiva, which I thought were those of lupus erythematosus.

DR. J. R. HASERICK: Many of you know the work being done by Hargraves. He reported finding lupus erythematosus cells in the bone marrow of acute

disseminated lupus erythematosus. My associates and I have reported finding the cell in 4 out of 5 cases of disseminated lupus erythematosus. The fifth case was of hemolytic anemia of the congenital type, and we felt that the bone marrow was altered. The diagnosis might be made in cases of lupus erythematosus in which there are no cutaneous changes, such as the second case today. When the patient first entered the hospital on the medical service the slight rash disappeared. About two or three weeks after admission Dr. Ernstene requested a bone marrow test. The patient did have large numbers of the lupus erythematosus cells in the bone marrow. Then she acquired lesions of the lips and of the mouth, which we felt were quite typical of lupus erythematosus. Some weeks after the bone marrow test she manifested a full blown dermatologic picture.

DR. J. R. DRIVER: Is there any explanation of the nature of the inclusion body?

DR. J. R. HASERICK: I think it is a megakaryocyte.

DR. E. W. NETHERTON: Dr. Haserick did not mention it, but in the first case he was unable to find the lupus erythematosus cell. However, he can take the blood from the first patient and add it to normal bone marrow and observe the same lupus erythematosus cell that he has been able to observe consistently for the other acutely ill patient.

Pemphigus Erythematodes. Presented by DR. GEORGE H. CURTIS.

Pemphigus Vulgaris. Presented by DR. GEORGE H. CURTIS.

Ocular Pemphigus. Presented by DR. E. W. NETHERTON.

Pemphigus Erythematosus (Senear-Usher Syndrome). Presented by DR. E. W. NETHERTON.

Mycosis Fungoides. Presented by DR. E. W. NETHERTON.

Monilethrix. Presented by DR. E. W. NETHERTON.

Extracellular Cholesterosis. Presented by DR. JOHN R. HASERICK.

Rosacea-Like Tuberculid. Presented by DR. E. W. NETHERTON.

A Case for Diagnosis: Lichen Sclerosus et Atrophicus? Lichen Planus Atrophicus? Presented by DR. U. W. LEAVELL, DR. J. J. STEWART and DR. J. G. THOMSEN (service of DR. H. N. COLE and DR. J. R. DRIVER).

Sarcoidosis in Identical Twins. Presented by DR. E. W. NETHERTON.

A Case for Diagnosis: Bromoderma? Presented by DR. GEORGE H. CURTIS.

LOS ANGELES DERMATOLOGICAL SOCIETY

Maxwell Wolff, M.D., *President*

J. R. Scholtz, M.D., *Secretary*

March 8, 1949

Porokeratosis of Mibelli. Presented by DR. M. E. OBERMAYER and DR. ERNEST FOX (by invitation).

E. B., a white man aged 49, has had a nonpruritic, slowly growing lesion on the dorsum of his right hand since childhood. The occurrence of similar lesions in other members of his family was denied.

Examination reveals on the dorsum of the right hand a plaque 5 by 7 mm. which has a fine, sharp, keratotic, slightly elevated border and atrophic center.

The sections showed a small ridge in the epidermis, with a central notch. Pronounced hyperkeratosis, moderate granulosis and dyskeratosis were present. Slight vascular dilatation, thickening of the intima and fibrocytic cellular infiltration were observed in the papillary and subpapillary portions of the dermis.

Keratoderma Circumscriptum or Porokeratosis of Mibelli? Presented by Dr. M. E. Obermayer and Dr. Ernest Fox (by invitation).

In 1934 C. F., a white woman aged 76, had a "wart" removed by electrodesiccation from the proximal portion of the right palm. At the same site a "callus" appeared and grew very slowly for years. In 1947 a dermatologist twice applied solid carbon dioxide to this lesion without causing its disappearance.

The patient was first seen by us in November 1948, at which time there was in the same location an elevated hyperkeratotic plaque approximately 1 cm. square. The possibility of a keratotic type of carcinoma was considered and a specimen for biopsy removed from the center of the lesion. The sections revealed in the epidermis pronounced hyperkeratosis accompanied with occasional areas of slight parakeratosis, irregular thickening of the granular layer and moderate acanthosis. Slight vascular dilatation and perivascular infiltration of round cells were present in the papillary and upper portions of the dermis. Migration of round cells into the lower two thirds of the epidermis was seen at one point.

During the following two months the lesion increased in size and in the irregularity of its outline. On Feb. 16, 1949, it was first observed that the border of the plaque had become slightly raised. Another specimen for biopsy was obtained, this time from the border of the more recently involved area. The sections showed decided hyperkeratosis, moderate granulosis and dyskeratosis in the epidermis; in the upper part of the dermis there were slight vascular dilatation and a perivascular cellular infiltrate, chiefly lymphocytes.

Examination reveals an irregular shaped hyperkeratotic plaque 2 cm. in diameter located on the most proximal portion of the right palm. The border is elevated approximately 1 mm.

Porokeratosis of Mibelli, Under Treatment with Solid Carbon Dioxide and Curettement and Desiccation. Presented by Dr. J. Walter Wilson.

W. L., a 40 year old white man, has had on his neck since infancy an abnormal plaque which he believes has changed only slightly over many years. He has been aware that the central portion of this lesion was smoother than the normal skin of his neck and that the border was irregularly circular and composed of hardened wartlike nodules. The lesion does not itch, but he admits picking at it frequently.

I first saw him in November 1948, at which time he presented on the left side of the nape a 3 cm. plaque, the center of which was moderately atrophic, with a border composed irregularly of acuminate nodules capped with horny keratin. A specimen taken for biopsy revealed acanthosis and hyperkeratosis as well as parakeratosis centering around the openings of sweat glands. The diagnosis of porokeratosis of Mibelli was made.

The patient was apprised of the innocous nature of the lesion but desired it be treated to avoid the tendency to excoriation. Several of the less keratotic areas of the border were successfully eradicated by the application of solid carbon dioxide. Recently three deeper areas have been treated by curettement and desiccation. The results to date have been satisfactory.

DISCUSSION OF CASES OF POROKERATOSIS

Dr. Kenneth Stout: The second case presented by Drs. Obermayer and Fox is the only one in which I entertained any doubt as to the diagnosis of porokeratosis. The other 2 cases microscopically showed the typical parakeratotic

cones and benign dyskeratosis. In the case I have doubts about there was a history of the taking of drops in water, in increasing and decreasing doses, over a period of months. If the preparation was potassium arsenite (Fowler's) solution, the possibility of an arsenical hyperkeratotic lesion must be considered.

DR. JOSEPH I. MIROVICH: Several months ago Dr. Samuel Ayres Jr. presented a yong boy who had had a porokeratosis of Mibelli lesion on the side of his neck for several years. Dr. Ayres prescribed vitamin A, 150,000 units daily, for about one year previous to the patient's presentation before this Society. There, was practically no evidence of the lesion at the time of presentation. I therefore wish to suggest that, if it has not been used, vitamin A in adequate doses be tried in the 3 cases now under discussion.

DR. ERNEST FOX: In 1947 Drs. Phyllis Jones and Dudley Smith of Charlottesville, Va., wrote a review of porokeratosis of Mibelli. The possible relation between vitamin A deficiency and this disease was discussed. The authors stressed the hyperkeratotic aspects of porokeratosis in its early stages but paid scant attention to the feature of benign dyskeratosis which Dr. George Andrews said he believed is the predominant characteristic of this disease. Large doses of vitamin A have proved to be beneficial in other dermatoses in which hyperkeratosis is a preeminent feature. Vitamin A has also been of value in Darier's disease, in which the feature of dyskeratosis is pronounced. It is possible that it may prove to be effectual in porokeratosis of Mibelli.

DR. M. E. OBERMAYER: While we were certain of the correctness of the clinical diagnosis in the man who presented the lesion on the dorsum of the hand, the clinical features of the plaque on the woman's palm were by no means typical of porokeratosis of Mibelli; it merely was a solid plaque with sharply defined borders progressing peripherally but did not exhibit the slender furrow in the peripheral wall with its hyperkeratotic ridge, which is generally considered essential. Nevertheless, the microscopic sections of the two lesions were practically identical. The question then arises whether the microscopic changes in dyskeratosis and "dislocation" of the sweat glands are suffiicent criteria for the diagnosis of porokeratosis in the absence of porokeratotic lamellas. I am inclined to think that they are.

DR. L. H. WINER: Pathognomonic of porokeratosis are the parakeratotic or coronoid lamellas of scales which look like a feather duster protruding from the sweat pore. Because of the location on the palmar skin, which abounds in sweat glands, I had expected to find greater involvement of sweat ducts than was found in the section. Clinically the lesions of both men felt soft, whereas the palmar lesions of the woman felt like scleroderma. However, the 2 cases presented by Drs. Obermayer and Fox were identical histologically. I agree with the diagnosis and prefer, as did Miescher, Resphigii's name of hyperkeratosis excentrica, or keradermia excentrica, for the condition. The inflammatory reaction under the epidermis involved by hyperkeratosis is characteristic of porokeratosis of Mibelli. The case of the woman reminds me of keratosis of palms and soles which has been linked morphologically recently with Kyrle's disease of folliculitis and perifolliculitis in cutem penetrans. These sections indicate the frequency of association of the nevoidal epidermal conditions associated with inflammatory processes.

DR. J. WALTER WILSON: I am sorry I did not present this man in December when he showed a typical picture of porokeratosis of Mibelli. This area had not changed for many years, presenting a smooth, soft center and hard, horny ridge. The area around the periphery which was treated is now soft, but it was

previously hard and warty. The center has not been treated as yet, except for the application of a little trichloroacetic acid on one occasion.

Hypertrophic Scar Formation Following Bullous Iododerma from Iodized Oil U. S. P. Presented by DR. M. E. OBERMAYER and DR. ERNEST FOX (by invitation).

Cavernous Hemangioma of the Breast in a 13 Month Old Infant. Presented by DR. CLEMENT E. COUNTER.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Frances M. Keddie, M.D., *President*

Otto E. L. Schmidt, M.D., *Vice President*

Rees B. Rees, M.D., *Secretary-Treasurer*

March 25, 1949

Coccidioidal Infection with Papulopustular Lesions. Presented (by invitation) by LIEUTENANT COLONEL ORLAND S. OLSEN, Medical Corps.

A Case for Diagnosis: Herpetic Cheilitis? Erythema Multiforme? Presented by DR. EDWARD A. LEVIN.

A Case for Diagnosis: Pemphigus? Erythema Multiforme? Presented by DR. JOHN M. GRAVES.

A Case for Diagnosis: Disseminated Lupus Erythematosus? Presented (by invitation) by DR. EDWIN M. HAMLIN.

Folliculitis Decalvans. Presented (by invitation) by LIEUTENANT COLONEL O. R. JENSEN, Medical Corps.

Sarcoidosis. Presented (by invitation) by LIEUTENANT COLONEL RAYMOND M. WILLIAMS, Medical Corps.

Lupus Erythematosus Profundus? Angiolupoid? Presented by DR. JAMES R. DRAKE.

Acanthosis Nigricans Juvenilis and Fragilitas Ossium. Presented by DR. HERBERT LAWRENCE.

Dermatomyositis with Spontaneous Improvement. Presented by DR. FRANCES A. TORREY.

Lymphoblastoma? Lichen Planus? Presented by DR. WALLACE PROCTOR.

Lupus Erythematosus? Presented by DR. WALLACE PROCTOR.

Lupus Miliaris Disseminatus Faciei. Presented by DR. ROBERT A. STEWART.

A Case for Diagnosis: Pseudoatrophoderma Colli? Presented by DR. ERVIN EPSTEIN.

A Case for Diagnosis: Psoriasis? Seborrheic Dermatitis? Presented by DR. H. V. ALLINGTON.

A Case for Diagnosis: Lupus Erythematosus? Lupus Vulgaris? Sarcoid. Presented by DR. CHARLES A. SHUMATE.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Archibald Gray, President, 39 Devonshire Place, London, W. 1.
Gordon B. Mitchell-Heggs, Secretary-General, Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle St., Leicester Square, London, W. C. 2.
Place: London. Time: Summer of 1952.

FOREIGN

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N. M. Wrong, Secretary, 604 Medical Arts Bldg., Toronto, Canada.

New Zealand Dermatological Society

P. E. Allison, President, 137 Cambridge Tce., "Harley," Christchurch.
R. G. Park, Secretary, Kelvin Chambers, 16 The Terrace, Wellington, C. I.

N. S. W. Branch of British Association of Dermatology and Syphilology

J. Witton Flynn, President, 175 Macquarie St., Sydney, N. S. W., Australia.
Richard B. Perkins, Secretary, 141 Macquarie St., Sydney, N. S. W., Australia.
Place: Royal Prince Alfred, St. Vincent's, Royal North Shore and Lewisham hospitals, Sydney, in rotation. Time: 4:00 p. m., last Friday in January, March, May, July, September and November.

North British Dermatological Society

President: Senior dermatologist in city where meeting is held.
A. Girdwood Fergusson, Secretary, 3 Ashton Rd., Glasgow W. 2, Scotland.

North of England Dermatological Society

A. Bigham, President, 6 Mornington Villas, Manningham Lane, Bradford.
G. Auckland, Secretary, 14 St. John St., Manchester 3.
Place: Manchester, Liverpool, Leeds, Sheffield and Bradford, in rotation. Time: Second Tuesday in April, May, June and October.

Royal Society of Medicine, Section of Dermatology

W. N. Goldsmith, President, 6 Upper Wimpole St., London, W. 1.
F. F. Hellier, Secretary, 20 Clarendon Rd., Leeds 2.
Place: Royal Society of Medicine, 1 Wimpole St., London W. 1. Time: 4:00 p. m., third Thursday of each month.

Sociedad Mexicana de Dermatologia

Roberto Nuñez Andrade, President, Milton 9, Mexico City.
Fernando Latapí, Secretary, Zacatecas, 220-6, Mexico City.
Place: National School of Medicine, Mexico City. Time: 9:00 p. m., first Thursday of each month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Clinton W. Lane, Chairman, 3720 Washington Ave., St. Louis, Mo.
John H. Lamb, Secretary, 117 N. Broadway, Oklahoma City, Okla.
Place: San Francisco. Time: June 26-30, 1950.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

Earl D. Osborne, President, 471 Delaware Ave., Buffalo 2, N. Y.
John E. Rauschkolb, Secretary, 25 Prospect Ave., Cleveland, Ohio.
Place: Palmer House, Chicago. Time: Dec. 2-9, 1950.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

F. E. Senear, President, 55 E. Washington St., Chicago 2.
George M. Lewis, Secretary, 66 E. 66th St., New York 21.

AMERICAN DERMATOLOGICAL ASSOCIATION

Charles C. Dennie, President, Professional Bldg., Kansas City, Mo.
Louis A. Brunsting, Secretary, 102—2nd Ave. S.W., Rochester, Minn.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY

Donald M. Pillsbury, President, 133 S. 36th St., Philadelphia 4.
Samuel M. Peck, Secretary, 140 E. 54th St., New York 22.
Place: San Francisco. Time: June, 1950.

SECTIONAL

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Officers are the same as those of the city where the annual meeting is held.

LONG ISLAND DERMATOLOGIC SOCIETY

Ida J. Mintzer, President, 88-50 163rd St., Jamaica 3, N. Y.
Conrad Stritzler, Secretary, 90-26 148th St., Jamaica 2, N. Y.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Francis P. McCarthy, President, 371 Commonwealth Ave., Boston.
Leonard E. Anderson, Secretary, Professional Bldg., Springfield, Mass.
Place: New Haven Hospital, New Haven, Conn., and Massachusetts General and Boston City hospitals (in alternation), Boston.

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

John P. Kiley, President, 94 Park St., Montclair, N. J.
Henri E. Abel, Secretary, 339 Union Ave., Elizabeth, N. J.
Place: Academy of Medicine, Newark, N. J. Time: 8:00 p. m., second Tuesday in October, November, January, March and May.

PACIFIC DERMATOLOGY ASSOCIATION

Harry J. Templeton, President, 3115 Webster St., Oakland, Calif.
Walter R. Nickel, Secretary, 233 "A" St., San Diego, Calif.
Place: Oakland, Calif. Time: Sept. 1-2, 1950.

PACIFIC NORTHWEST DERMATOLOGICAL SOCIETY

Robert L. Howard, President, Paulson-Medical-Dental Bldg., Spokane, Wash.
Leon F. Ray, Secretary, 628 Medical Dental Bldg., Portland 5, Ore.
Place: Place varies. Time: Third Thursday of May and October.

ROCKY MOUNTAIN DERMATOLOGIC SOCIETY

G. P. Lingenfelter, President, 910 Republic Bldg., Denver, Colo.
David J. Musman, Secretary, 1024 Republic Bldg., Denver, Colo.
Place: Selected prior to each meeting. Time: Selected prior to each meeting.

SOUTHEASTERN DERMATOLOGICAL ASSOCIATION

A. H. Lancaster, President, 608 W. Main Ave., Knoxville, Tenn.
Leon Bryan, Secretary, Doctors Bldg., Columbia, S. C.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Richard W. Fowlkes, President, 701 Professional Bldg., Richmond 19, Va.
D. Truett Gandy, Secretary, 424 Medical Arts Bldg., Houston 2, Texas.

SOUTHWESTERN DERMATOLOGICAL SOCIETY

Leslie M. Smith, President, First National Bank Bldg., El Paso, Texas.
George K. Rogers, Secretary, Lois Grunow Memorial, Phoenix, Ariz.

STATE

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

Maximilian E. Obermayer, President, 2007 Wilshire Blvd., Los Angeles 5.
Werner W. Duemling, Secretary, 3367—4th Ave., San Diego, Calif.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY

Albert Levenson, President, 881 Lafayette St., Bridgeport, Conn.
Louis O'Brasky, Secretary, 1172 Chapel St., New Haven, Conn.
Place: New Haven, Conn.

FLORIDA ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY

Lauren M. Sompayrac, President, 459 St. James Bldg., Jacksonville.
Wesley W. Wilson, Secretary, 1122 Citizens Bldg., Tampa.

HAWAII DERMATOLOGICAL SOCIETY

Harry L. Arnold Jr., Secretary, 881 S. Hotel St., Honolulu 53.
Place: 881 S. Hotel St., Honolulu. Time: Every three months when possible.

LOUISIANA DERMATOLOGIC SOCIETY

Barrett Kennedy, President, Hibernia Bank Bldg., New Orleans.
V. Medd Henington, Secretary, 607 American Bank Bldg., New Orleans.
Place: Charity Hospital, New Orleans. Time: Fourth Sunday of each month.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Austin W. Cheever, President, 464 Beacon St., Boston.
Maurice M. Tolman, Secretary, 636 Beacon St., Boston.
Place: Hotel Statler, Boston.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Maurice J. Costello, President, 140 E. 54th St., New York 22.
William F. Hoover, Secretary, 11 Physician's Bldg., Jamestown.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Herman Beerman, President, 255 S. 17th St., Philadelphia.
Thomas Butterworth, Secretary, 411 Walnut St., Reading.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

John H. Cobane, President, 10 Peterboro, Detroit 1.
Herbert H. Holman, Secretary, 2010 David Broderick Tower, Detroit 26.

MINNESOTA DERMATOLOGICAL SOCIETY

Robert R. Kierland, President, 102—2nd Ave., S.W. Rochester.
Elmer T. Ceder, Secretary, 652 Medical Arts Bldg., Minneapolis 2.

OKLAHOMA DERMATOLOGICAL ASSOCIATION

W. A. Showman, President, 409 Medical Arts Bldg., Tulsa.
Phyllis E. Jones, Secretary-Treasurer, 705 Medical Arts Bldg., Oklahoma City 2.
Place: Oklahoma City and Tulsa. Time: Spring and Fall.

TEXAS DERMATOLOGICAL SOCIETY

William A. Clark, President, 1215 Walker Ave., Houston 2.
W. Harris Connor, Secretary, 1215 Walker Ave., Houston 2.
Place: Rotating. Time: Spring, coincident with Texas State Medical Association; fall, October.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Harry M. Robinson, Jr., President, 1025 N. Calvert St., Baltimore 2, Md.
Israel Zeligman, Secretary, 1109 N. Calvert St., Baltimore 2, Md.
Place: Baltimore and Washington. Time: Third Thursday of each month in alternate cities, October to May.

BRONX DERMATOLOGICAL SOCIETY

Charles F. Sims, President, 1840 Grand Concourse, Bronx.
Henry Silver, Secretary, 290 West End Ave., New York.
Place: Academy of Medicine. Time: Third Thursday of every month, October to May.

BROOKLYN DERMATOLOGICAL SOCIETY

E. Almore Gavuain, President, 80 Hanson Place, Brooklyn.
Samuel I. Greenberg, Secretary, 277 Eastern Pkway., Brooklyn 16.
Place: Brooklyn Hospital Dispensary, Ashland Place, Brooklyn. Time: Third Monday of each month, October to May.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Shepard Quimby, President, 287 Linwood Ave., Buffalo.
Frank A. Dolce, Secretary, 468 Delaware Ave., Buffalo.
Place: Edward J. Meyer Memorial Hospital, Buffalo, and Strong Memorial Hospital, Rochester, N. Y. Time: Second Tuesday of every month, October to May, inclusive.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Maxwell C. Snider, President 106 Oak St., Binghamton.
John Copeland, President, 220 Lancaster St., Albany.

CHICAGO DERMATOLOGICAL SOCIETY

Carl W. Laymon, President, 78 S. 9th St., Minneapolis
James R. Webster, Secretary, 122 S. Michigan Ave., Chicago 3.
Place: Chicago. Time: Third Wednesday of each month except June, July, August and September.

CINCINNATI SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Lawrence C. Goldberg, President, Doctor's Bldg., Cincinnati.
John B. Squires, Secretary, 1023 Carew Tower Bldg., Cincinnati.
Place: Cincinnati General Hospital, Cincinnati. Time: 8:15 p. m., first Wednesday of each month, October to May.

CLEVELAND DERMATOLOGICAL SOCIETY

Emerson Gillespie, President, 721 First National Bank Bldg., Canton.
H. H. Johnson, Secretary, 10515 Carnegie Ave., Cleveland 6.
Place: Various local hospitals. Time: Fourth Thursday of each month, September to May.

DETROIT DERMATOLOGICAL SOCIETY

Frank Stiles, President, 2012 Olds Tower, Lansing 2.
Herbert H. Holman, Secretary-Treasurer, 2010 David Broderick Tower, Detroit 26.
Place: Local hospitals in Detroit and vicinity. Time: Third Tuesday of each month except June, July, August and September.

Kansas City (Mo.) Dermatological Society

J. Paul Frick, President, 800 Professional Bldg., Kansas City.
David B. Morgan, Secretary, 520 Professional Bldg., Kansas City.
Place: University of Kansas Medical Center. Time: 10 a. m., second Sunday of each month from October through June.

Los Angeles Dermatological Society

Jud R. Scholtz, President, 950 E. Green St., Pasadena.
Molleurus Couperus, Secretary, 1930 Wilshire Blvd., Los Angeles 5.
Place: Good Hope Clinical Association. Time: Second Tuesday of each month, October to May.

Manhattan Dermatologic Society

Maurice J. Costello, President, 140 E. 54th St., New York 22.
Wilbert Sachs, Secretary, 6 E. 85th St., New York.
Place: Each member's office in rotation. Time: 8:00 p. m., second Tuesday of each month.

Metropolitan Dermatological Society

Joseph C. Amersbach, President, 105 E. 53rd St., New York.
Valentine C. Baker, Secretary, 619 W. 140th St., New York.
Place: Offices of members. Time: Third Monday of each month, October to May.

Metropolitan Dermatological Society of Los Angeles

David N. Alcon, President, 2007 Wilshire Blvd., Los Angeles.
Harold C. Fishman, Secretary, 105 N. Vincente Blvd., Beverly Hills.
Time: Fourth Tuesday of each month, October through May.

Montreal Dermatological Society

Donald S. Mitchell, President, 1414 Drummond St., Montreal, Quebec.
Georges Leclerc, Secretary, 418 Sherbrooke St. E., Montreal, Quebec.
Place: Royal Victoria Hospital, Notre Dame Hospital, Montreal General Hospital and other hospitals. Time: October, February and April.

New York Academy of Medicine, Section of Dermatology and Syphilis

George M. Lewis, President, 66 E. 66th St., New York 21.
Marion B. Sulzberger, Secretary, 962 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St., New York.

New York Dermatological Society

George M. Lewis, President, 66 E. 66th St., New York 21.
John C. Graham, Secretary, 80 Hanson Pl., Brooklyn.
Place: New York. Time: Fourth Tuesday of each month.

Omaha Dermatological Society

Zeno K. Korth, President, 1319 Medical Arts Bldg., Omaha.
George F. Pinne, Secretary, 453 Aquila Court, Omaha.
Time: Third Wednesday of each month, September to June.

Philadelphia Dermatological Society

Robert L. Gilman, President, U. S. Naval Hospital, Philadelphia.
H. E. Twining, Secretary, 2026 Delancy Place, Philadelphia 3.
Place: Philadelphia hospitals. Time: Third Friday of each month except June, July and August.

Pittsburgh Dermatological Society

H. W. Woolhandler, President, Jenkins Arcade, Pittsburgh.
P. V. Graham, Secretary, 40 14th St., Wheeling, West Virginia.
Place: Falk Clinic, 3601 Fifth Ave., Pittsburgh. Time: Evening of third Thursday of each month except July and August.

ST. LOUIS DERMATOLOGICAL SOCIETY

Garold V. Stryker, President, 634 N. Grand Blvd., St. Louis.
Morris Moore, Secretary, 3427 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 8:00 p. m., third Monday of each month, October to May.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Robert A. Stewart, President, San Francisco.
Rees B. Rees, Secretary-Treasurer, 384 Post St., San Francisco.

ST. LOUIS DERMATOLOGICAL SOCIETY

Garold V. Stryker, President, 634 N. Grand Blvd., St. Louis.
Morris Moore, Secretary, 3427 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 8:00 P. M., third Monday of each month, October to May.